

Mellina da Silva Terres
Silvio César Cazella
Alexandre Bonatto *Editors*

Applied Interdisciplinary Research: Integrating Information Technologies and Health

Moriá Editora

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**APPLIED INTERDISCIPLINARY RESEARCH:
INTEGRATING INFORMATION
TECHNOLOGIES AND HEALTH**

ACKNOWLEDGMENT

We would like to especially thank to Mellina da Silva Terres for her dedication and support to the Postgraduate Program in Information Technologies and Health Management (PPGTIGSaúde) at the Federal University of Health from Porto Alegre, which, based on so many efforts, culminated in the creation of this book of an interdisciplinary nature, as well as the Rio Grande do Sul Research Support Foundation (FAPERGS) which, through Edital 18/2020 - Support for Emerging and Consolidation Postgraduate Programs in Priority Areas in the States - included PPGTIGSaúde (grant term number 21/2551-0000513-0) with a resource that supports development of this work.

Finally, we would like to thank the authors who made this publication possible and the readers who will enable the application of the knowledge presented here.

PREFACE

The transition from Society 4.0 to Society 5.0 represented a profound transformation in how we relate to technology, especially regarding the massive and constant use of computers and mobile devices. Society 5.0 seeks to balance technological advancement and the improvement of quality of life through a more conscious and humanized use of technology in the search for solutions that promote social and emotional well-being.

Although this technological evolution has resulted in fast connectivity and the availability of internet access in any location on the planet, it has also imposed significant challenges and the urgent need to work in an integrated and interdisciplinary manner to seek solutions or ways to mitigate its impacts. Here, we refer to climate change, which represents one of the greatest challenges for future interdisciplinary research, as its consequences affect various areas of knowledge, including, for example, natural, social, economic, and health sciences. One of the main obstacles is the need for collaboration between different disciplines, which often have distinct approaches and terminologies, creating challenges such as communication and data integration, thus complicating the development of effective solutions, while also offering opportunities for the integration of different bodies of knowledge.

One of the cities affected in the state of Rio Grande do Sul by climate change in May 2024 was Porto Alegre, the city where the Federal University of Health Sciences of Porto Alegre (UFCSA) is located. Given UFCSA's important role in assisting the affected population, it is clear that, after this calamity, research that supports the state, especially in the health field, cannot be conceived without placing interdisciplinarity at its core.

It became evident that the need for different bodies of knowledge was critical to addressing such a complex situation, where both the population and the state's economy were strongly impacted by the interruption of essential services, such as water supply, electricity, and transportation.

Interdisciplinary research is fundamental in the health sector, as it allows for the integration of knowledge and practices from different fields, such as medicine, biology, psychology, sociology, engineering, among others. This collaborative approach enriches the understanding of complex problems, such as chronic diseases and epidemics, enabling the development of more comprehensive solutions. By uniting various fields,

interdisciplinary research fosters innovation, for example, in treatments and public health policies, for the benefit of human well-being.

The United Nations (UN) established the Sustainable Development Goals (SDGs), defining a global agenda aimed at addressing social, economic, and environmental challenges by 2030. There are a total of 17 goals that cover issues such as poverty eradication, quality education, gender equality, and climate action, requiring a collaborative, multidisciplinary, and interdisciplinary approach. Interdisciplinary research can play a crucial role in achieving these goals, as it promotes collaboration between different areas of knowledge, allowing for a more comprehensive and effective analysis of problems and solutions.

The *APPLIED INTERDISCIPLINARY RESEARCH: INTEGRATING INFORMATION TECHNOLOGIES AND HEALTH* presents twenty chapters on interdisciplinary research, where the Sustainable Development Goals (SDGs) are identified, authored by faculty, researchers, and students from the Graduate Program in Information Technologies and Health Management (PPGTIGSaúde) at UFCSPA, as well as external collaborators. This book is the second publication of the program, which is an academic master's program linked to the Health and Biological Sciences Chamber and the Interdisciplinary area of CAPES. This book presents research conducted in the program on current topics related to the research lines of Intelligent Systems and Applications in Health and Information and Knowledge Management in Health.

Thus, this book reflects the importance of interdisciplinary research as an essential path to address contemporary challenges, particularly in the context of health and technology. May it serve as inspiration for new studies, collaborations, and solutions that contribute to a more sustainable, equitable, and connected world.

Profa. Dra. Jenifer Saffi
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Internationalization of the Federal University of
Health Sciences of Porto Alegre (UFCSPA)

We dedicate this work to scientists, professionals who work with interdisciplinarity, seeking the integration of different disciplines or fields of knowledge to address complex issues and challenges that cannot be fully understood through a single disciplinary perspective.

into dashboards for analyzing scenarios like infectious diseases and pediatric oncology. Chapter 2, led by Liége Caroline Immich, explores the role of an anesthesia information management system in enhancing the perioperative process by monitoring patient progress from surgical consultation to hospital discharge, alongside discussing digital health platforms' impact on improving preoperative assessments and surgical outcomes.. In Chapter 3, Ariel Castro Bacchieri and colleagues present strategies and characteristics of digital health initiatives aimed at promoting health equity for Black people in Brazil, addressing the challenges posed by structural racism. Chapter 4, authored by Natália Marmitt and others, discuss how technologies like data mining and artificial intelligence address the complexities imposed by abundant and heterogeneous health data, enhancing management and care in healthcare, particularly in oncology. Chapter 5, by Giordani da Silva Ramos and Ana Beatriz Gorini da Veiga, discusses the challenges of extracting and interpreting health data from digital platforms, emphasizing the need for continuous improvement in data analysis and governance policies to handle complexities related to data quality, interoperability, healthcare diversity, legal issues, and the rapid growth of data volumes in integrated health information systems.

Chapter 6, led by Felipe Boeing Pinheiro, discusses the use of Additive Manufacturing (AM) in hospitals during the COVID-19 pandemic to address medical equipment shortages, exploring its integration with biocidal materials and the implications for budget and health management in overcoming supply chain disruptions. In Chapter 7, Emanuele König Klever and co-authors propose a model for designing health information and communication technologies (ICTs) that better meet the needs of users facing limitations. Chapter 8, by Melina da Costa Oliveira and Otávio Neves da Silva Bittencourt, explores the effective use of instant messaging in enhancing interdisciplinary communication in healthcare settings. Chapter 9, authored by Sheron Tannara Vargas and team, covers patient navigation and telenursing in cancer care, highlighting the integration of information technologies. Finally, Chapter 10, by Enio Rodrigo Fernandes Rodrigues, examines the dosimetric properties of VHEE-FLASH radiotherapy in treating hypoxic tumors, offering insights into its potential clinical applications.

In Chapter 11, Cecilia Dias Flores and co-authors delve into clinical decision support systems based on probabilistic networks, focusing on their impact on healthcare decision-making. Chapter 12, led by Letícia Fröhlich, discusses radiobiological parameters in prostate cancer radiotherapy,

analyzing treatment planning and outcomes. Chapter 13, by Vanessa Klimkowski Argoud and colleagues, explores the integration of telepharmacy in pharmaceutical care, highlighting its potential in enhancing patient experience. Chapter 14, authored by Natália Fernandes and colleagues, analyzes the application of the Lean methodology to streamline the electrotherapy process in a complex hospital setting, using a case study that employs value stream mapping to enhance efficiency and patient care outcomes.

In Chapter 15, Jonathan Alexander Prestes Fruscalso and co-authors introduce an optimization algorithm designed to achieve a homogeneous dose deposition along a given tumoral region for the focused very high-energy electron (VHEE) radiotherapy. Chapter 16, by Samara Prass dos Santos and colleagues, investigates the optimization of laser-plasma accelerators, using Bayesian optimization to enhance the production of the radioisotope ^{99}Mo through photoactivation, presenting an alternative to traditional uranium fission in nuclear medicine. Chapter 17, led by Silvio César Cazella, presents mHealth applications, including a Digital Vaccination Card, discussing its role in public health management. Chapter 18, authored by Alexandro Ferreira Guimarães and co-authors, explores Monte Carlo codes for microdosimetric simulations in radiotherapy. Chapter 19, by Caio dos Santos Felipe and colleagues, discusses an AI model for classifying brain tumors, emphasizing the importance of Explainable AI in medical diagnostics. Finally, in Chapter 20, Silvio Cazella and his colleagues report some of the main challenges associated with the proposal and implementation of PPGTIGSaúde, the first interdisciplinary graduate program at the Federal University of Health Sciences of Porto Alegre (UFCSA).

The book emerges as a reflection of PPGTIGSaúde's innovative interdisciplinary approach, encapsulating the thoughts and research of its community. We hope that readers find both enjoyment and inspiration as they explore the connections of information technologies and health presented within these pages.

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1 Data Analytics and Visualization in Healthcare Decision-Making: Examples, Benefits & Challenges Related to Epidemiological Scenarios

Isabel Cristina Siqueira da Silva
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Abstract:

Data visualization techniques applied to healthcare can help convert complex data into visual resources that aid understanding for stakeholders, whether they are doctors, patients, or government officials. For the epidemiological scenarios, the analytical and interactive visualization of data, grouped into dashboards, allows integration between different databases. This chapter addresses the role of data analytics visualization in epidemiologic scenarios and how the application of analytical data visualization techniques can help managers and healthcare professionals in decision-making process. We discuss three different case studies related to the spread of infectious diseases, to the analysis of data related to pediatric oncology and how analytical visualization was proposed as a tool to help identify patterns and generate insights in relation to the specific data of each case.

Keywords: Data visualization; data analytics; healthcare; decision making; epidemiology.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

1.1 Introduction

Data analysis and visualization applied to healthcare decision-making can significantly contribute to the epidemiological scenarios and to the process of managing the patient's journey throughout the entire process, from making a diagnosis to the post-treatment period [Craft et al. 2015] [Stadler et al. 2016] [Franklin et al. 2017] [Chinnaswamy et al. 2019] [Afzal et al 2020] [Park et al. 2022] . However, effective use of these data faces substantial challenges due to their heterogeneity and diversity, in addition to unstructured health records. Issues such as lack of standardization, variability in data quality and privacy concerns emerge as critical obstacles to overcome.

Moreover, while governments at various levels are responsible for defining and implementing measures to mitigate the effects of epidemiological scenarios, citizens must be informed to understand the breadth of actions needed to curb the spread of diseases, accepting, and adhering to such measures. The media have played an essential role in providing information about how different diseases are occurring in countries and how each can help control it. Generally, epidemiological data and statistics are analyzed and discussed through textual tables, linear and bar charts. The abstraction present in such data display methods may not be effective in communicating information, especially considering the public and key stakeholders. It is also too simple for data analysis to support decision making targeting public policies applied in the cities. This aspect is crucial when decisions must be made in a very expeditious way.

Intuitive reasoning plays a critical role when decisions must be made across a wide spectrum of social agents. Therefore, very abstract information may not help citizens understand the importance of prevention and control of epidemiological, demographic, institutional scenarios, etc. This is not a new problem: semiology has been used to improve levels of public awareness over aspects such as the danger of collisions, environmental accidents, etc., through visual communication employing signs and different sorts of images conveying warnings and general information. Humans have the capacity to translate these signs into shared and consensual behavior. Unfortunately, complex data face clear difficulties to be intuitively grasped.

In this context, data visualization plays a significant role in shortening the time between data analysis and the implementation of practical measures. When one should consider issues that involve analytical

reasoning combined with data visualization, visual analytics techniques are needed. A key aspect of visual analytics is that it is highly interdisciplinary, integrating data visualization, data mining, data management, data fusion, statistics, and cognitive science [Keim et al. 2008] [Ware 2019]. Human and social health studies received a special contribution from geospatial technologies, specifically in the field of spatial epidemiology.

This chapter addresses the role of data analytics visualization in different scenarios and how the application of analytical data visualization techniques can help managers and healthcare professionals in decision-making process. We discuss three different case studies related to:

- Analysis of data related to spread of infectious diseases;
- Analysis of data related to pediatric oncology; and
- Analysis of data related to cardiovascular response of children to microgravity simulation).

These three different case studies were specially chosen to be presented in this chapter in order to exemplify how the area of analytical data visualization can help identify patterns and generate insights in relation to specific data from the most varied study areas.

The remainder of the chapter is organized as follows. Section 1.2 presents the case study related to the analytics visualization of spatio-temporal data related to the spread of infectious diseases in 3D cities models. Section 1.3 presents the case study related to the analytics visualization applied to pediatric oncology data: investigation of epidemiological patterns. Section 1.4 presents the case study related to the analytics visualization of dData related to cardiovascular response of children to microgravity simulation. Finally, the results are discussed in Section 1.5, which also presents our final comments.

1.2 Analytics Visualization of Spatio-Temporal Data Related to the Spread of Infectious Diseases in 3D Cities Models

A disease becomes a pandemic when it reaches global levels, that is, when a certain agent spreads across several countries or continents, usually affecting many people. The World Health Organization (WHO) defines when a disease becomes this type of global threat [WHO 2020]. A pandemic may begin as an outbreak or epidemic; that is, outbreaks, pandemics and epidemics have the same origin - what changes is the scale of the disease's spread.

In a pandemic scenario, a 3D representation of an area of the city where a citizen lives, and that has a high level of contagious virus presence, tends to impact this more profoundly than the display of generic bar and line graphs. If the 3D images of a region of the city are analyzed in parallel with a 2D representation of the surroundings of this region, both images will complement each other, bringing the benefits of the typology task based on overview+detail to interact with spatio-temporal data representations.

The 2D and 3D modeling of the city should cover all relevant aspects to the problems that require smart solutions, as networks and flows that can describe all movements in the city, models of buildings and facilities, including all aspects that could impact the city, its environment, its citizens and their activities, capable of supporting planning and maintenance through spatio-temporal data, aspects of urban planning, environmental factors, etc. [Carroll 2014] [Silva et al. 2020] [Dübel 2024] 3D city models, specifically, represent an approximation of the real world, where the quantity and content of a city model is directly related to the usage of the 3D model and time which generate 4D visualizations.

Herein, the research discussed in this section is related to a visual analytics solution applied to spatio-temporal data from city locations where people were during the asymptomatic infectious period before having confirmation of being infected with a specific disease. We assume that the territorial model of cities allows the identification of the urban areas most subject to the risk of infectious virus dissemination. Such identification can assist decision-making within the management performed by the city government, to plan the restrictions imposed by the risk of the rapid spread of the disease, identifying and mapping the areas of the city (with an accuracy of land or building) where efforts should be concentrated on prevention actions. This issue is particularly important when considering the migration of the infectious disease virus from the periphery to large urban centers.

As an initial case study, we applied the proposed model to analyze the spread of COVID-19 in the city of Porto Alegre, Brazil, and validate the results with experts from different scientific fields. In summary, the main contributions of this approach are:

- To provide 2.5D, 3D and 4D visualizations of potential disease dissemination points in urban areas based on spatio-temporal data related to coincidence locations of infected citizens;

- To help the understanding of the routes and timings of transmission to engage governments and citizens to contribute to the fight against pandemics;
- To support health surveillance and social distancing policies assisting decision making by public managers considering categories of activities in the urban scenario of smart cities.
- To allow the description of territorial characteristics of the dissemination of infectious diseases in neighborhoods, cities, and metropolitan regions.

We interviewed specialists of local scientific committees for the COVID-19 pandemic and about twenty experts from state secretaries of health and health surveillance to understand the main tasks and elements that they analyze when defining strategies to contain the circulation of the virus. The interviews were structured and performed with video-conference tools due to the isolation measures at the time. The questions asked to the specialists were:

1. In a pandemic scenario, what are the main aspects considered for planning public policies related to social distancing to reduce contagion in cities?
2. What are the main tasks performed on the COVID-19 spatio-temporal data needed to understand the outbreak of the virus and plan public policies aimed at reducing contagion in cities?
3. What visualization and interaction resources related to the spatio-temporal data in the cities are more intuitive and effective for understanding the spread of infectious diseases?
4. Once the areas of the city with the greatest circulation of viruses are identified, what the main tasks and strategies to contain the virus need to be carried out?

According to specialists, the main tasks performed by them on the COVID-19 spatio-temporal data are:

- Analyze the movements of infected people (individual or group) across the city in a specific time interval (not necessarily a specific route/trajectory, as it varies across cities, but the origin and target locations);

- Identify places of coincidence of visitation by at least two infected people (coincidence degree), in a time interval, for diverse activity categories in the urban scenario;
- Interact with multiple and coordinate views in order to allow the visualization of overview+details of coincidence locations and agents' movements, being able to filter these in order to avoid cognitive overload;
- Allow data analysis, viewing dashboards referring to the crossing of data involving places of coincidence, time interval, number of infected people, degrees of coincidence of places, etc.

Based on these aspects, we defined the goals of our research as follows:

- To provide a visual analytics solution relating the potential disease outbreak points in urban areas to spatiotemporal data of coincidence locations of infected people during the asymptomatic infectious period;
- To support health surveillance and social distancing policies assisting decision making by public managers based on an intuitive visualization of the aforementioned spatiotemporal data;
- To represent the territorial characteristics of the dissemination of infectious disease in neighborhoods, cities, and metropolitan regions from the number of infected people and their movement in these areas.

Then, we employ 2.5D arcs for representing the infected person's specific movement between a place of origin and a place of destination in the city without interfering with the display of the city element's connection (Figure 1 (a)). The 2.5D arcs aggregate trajectories into flows, assuming that each trajectory represents a full trip of a moving object from some origin to some destination. The arcs projected over the city model help us to analyze the dimension hops, scope, and direction.

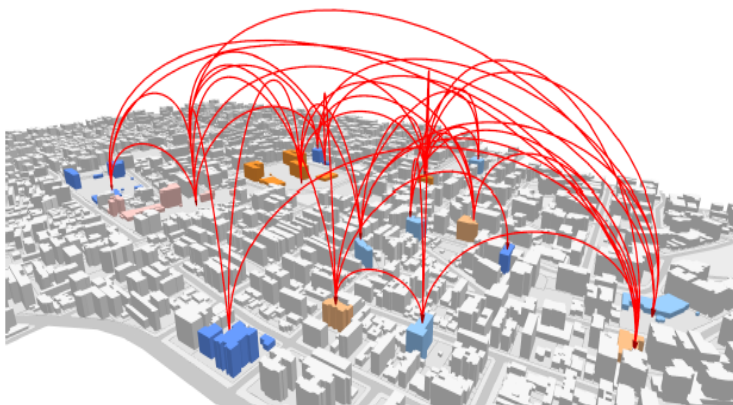
The arcs can be filtered to show one or more persons, allowing individual analysis of movements, and avoiding possible cognitive overload when there is a high number of movements in the same region of the city. Each person is generically referenced by an agent ID to preserve their privacy. Alternatively, the agent's movements between origin and target points can be displayed as a 2D visualization to reduce the cognitive

overload for a large area (Figure 1 (b)). In this visualization, the movements are exhibited as 2D red lines over the XZ-plane.

The user can switch between 2D or 3D viewing or see both together through multiple and coordinated views, a typical interaction resource present in city visualization systems and in solutions based on overview+detail techniques. The user can apply zoom, pan, and rotation in the scene as well as filtering it by different attributes. Colors and shades indicate the intensity of occurrences of diagnosed infectious disease cases, while locations can be mapped by categories within cities, such as schools, restaurants, supermarkets, etc., as shown in Figure 1 (c).

The experts were unanimous in indicating the advantages they would have in applying our solution in practice, especially considering the need for a gradual and controlled return to the operation of services (education, commerce, leisure, etc.). They said the most significant risk of spread is that many people have no idea that they are infected, which increases a pandemic situation. Thus, identifying the places infected people visited is essential for understanding the spread of the disease in cities, which is the main contribution of this work.

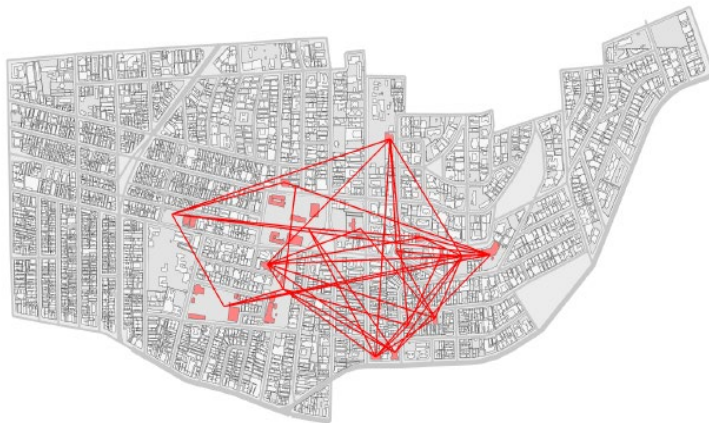
Figure 1. Data visualizations related to a specific disease outbreak: (a) occurrence of cases diagnosed with a specific infectious disease; (b) 2D visualization of agent's movements in a specific region of the city; and (c) Mapping the occurrence of confirmed cases of a disease categorized by restaurants in a city.



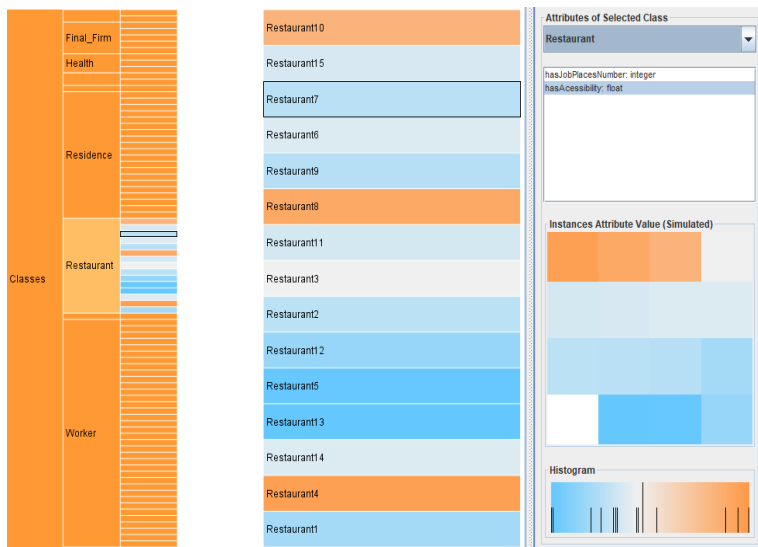
(a)

1 Data Analytics and Visualization in Healthcare Decision-Making: Examples, Benefits & Challenges Related to Epidemiological Scenarios

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(b)



(c)

1.3 Analytics Visualization applied to Pediatric Oncology Data: Investigation of Epidemiological Patterns

The second case study is related to the pediatric oncology data, where we have a scenario in which the 5-year survival rate of children and adolescents diagnosed with cancer is approximately 80% in high-income countries. These estimates are much worse in low- and middle-income countries, where more than 80% of children with cancer live [INCA 2022] [INCA 2023]. Due to improvements in the treatment of infectious and non-communicable diseases in these countries, cancer treatment has become a focus as it is one of the main causes of death in children and adolescents.

In Brazil, childhood cancer is the leading cause of death from disease in children aged 1 to 19 years, surpassing infectious diseases. The National Cancer Institute (*Instituto Nacional do Câncer* - INCA) estimates that more than 7,000 new cases of pediatric cancer will occur in Brazil in 2023, with an estimated survival rate of 64%, combined with a huge disparity between regions [INCA 2023]. Children's tumors differ from those of adults in terms of their morphological aspects, clinical behavior, and primary locations and, therefore, must be studied and treated separately.

Children treated in pediatric oncology centers have an 80% chance of cure, whereas when they are treated in adult protocols and centers the chance of cure drops to 40% [INCA 2022] [INCA 2023]. The chances of an effective cure for childhood cancer will also depend on the type of cancer and are closely related to the ability to diagnose early and accurately, treatment within clinical protocols and a multidisciplinary team specialized in pediatric oncology and effectiveness in detecting metastatic or relapsed disease. Other factors such as poor access to comprehensive patient care, late diagnosis, inadequate educational programs, lack of protocol-based decisions and center expertise, unavailability of multidisciplinary teams, differences between states, scarcity of public resources and specific government policies also play a critical role in the quality of treatment for these patients.

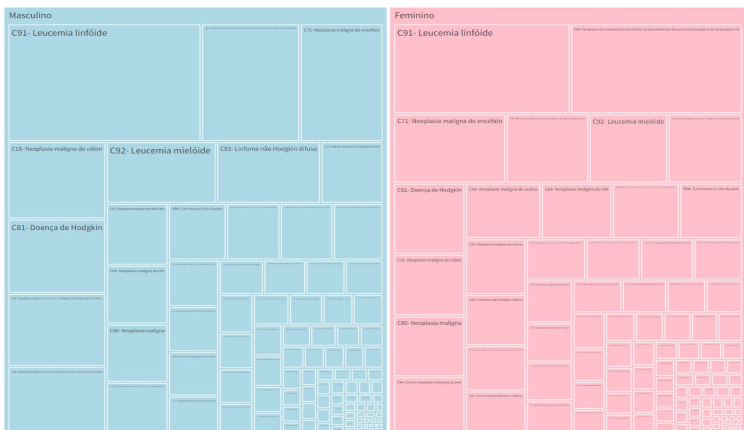
In pediatric oncology, we face considerable obstacles in the construction of a comprehensive and accurate epidemiology. This is largely due to the incongruous nature of data records and the complexities involved in collecting them. The crucial steps of recording and collecting information often face challenges, as those responsible do not always fully understand the importance of each piece of information collected. The lack of feedback on the use of this data in the construction of public policies can lead to a

gap in this understanding. However, it is vital to recognize that data constitutes the starting point for developing any policy, strategy, or program, regardless of the area of activity, including health.

In this sense, clinical dashboards can make a big difference in supporting population health management, facilitating real-time monitoring, with the help of data that goes beyond the international classification of diseases 11th revision (ICD-11), which was implemented for mortality coding and classification from death certificates in the U.S. in 1999, and other medical terminologies. Clinical dashboards enable population health managers to make decisions based on data rather than intuition. They provide clear insight into patients and their clinical data, which makes it easier to identify problems and implement solutions.

In relation to childhood cancer data, we are investigating visualization techniques and forms of interaction to build a clinical dashboard that integrates different pediatric oncology databases. One of the techniques listed and under evaluation is the treemap (Figure 2), related to the distribution of male and female genders by confirmed diagnosis. In the visualization, the colors represent the genders, and the sizes of the rectangles represent the number of confirmed cases of the disease according to the type of tumor aiming to assist in the identification of patterns.

Figure 2. Data distribution of male and female genders by confirmed diagnosis



Besides, we are testing the sunburst chart (Figure 3) to analyze the types of tumors diagnosed and the treatment time carried out for each of them. A sunburst graphic highlights hierarchy through concentric rings. Each ring is a level of the hierarchy and provides a sense of the entire relationship of that segment to the parent node.

These first tests with interactive visualizations were analyzed by stakeholders who contributed to this study, and all highlighted the benefits that such proposals bring to the analysis of pediatric oncology data. Some evaluators pointed out that the information presented in the sunburst chart, due to the variety of tumor types, ends up overlapping and makes individual identification of occurrences somewhat difficult. However, they approve of the visual synthesis used for the analysis of different types of tumors, which is usually carried out using text tables, generating cognitive overload and difficulty in obtaining quick insights.

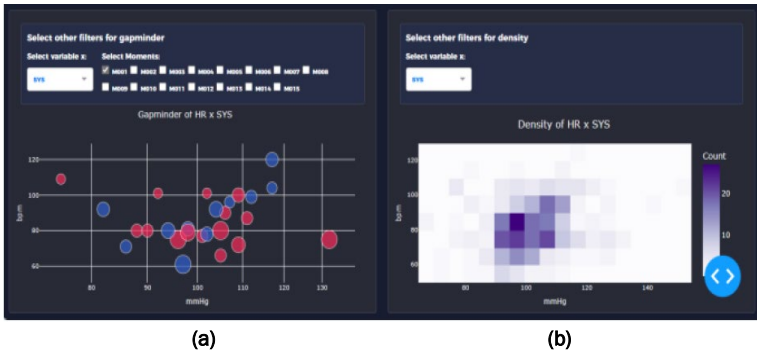
1.4 Analytics Visualization of Data Related to Cardiovascular Response of Children to Microgravity Simulation

The third case study refers to the cardiovascular response of children to microgravity simulation related to space exploration. Space exploration is challenging because important environmental factors continue to be constant threats to the health and well-being of astronauts, such as microgravity, radiation, confinement and isolation [Grigoriev et al. 2011] [Baran et al. 2022]. Many aspects related to cardiovascular adaptation during a space mission have been studied, but mostly focused on adults.

However, the rise of space tourism will also likely see the participation of children, for which there is a complete lack of data related to how they might respond to the space environment. Considering these aspects, we are investigating analytical visualization techniques that assist in data analysis related to cardiovascular response of children to microgravity simulation.

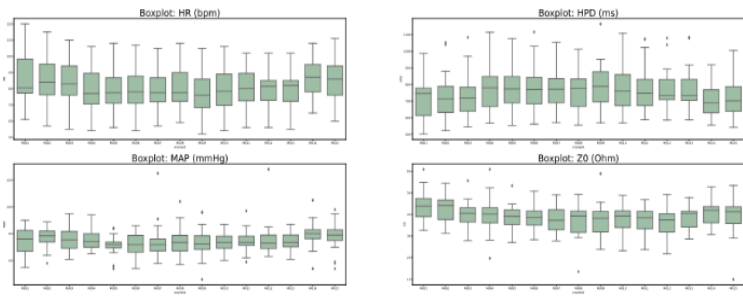
We are developing an interactive dashboard for visual analysis of this data that incorporates the gapminder visualization (Figure 4), which generates graphs based on interactive scatterplot, and pixel-oriented charts related to the data density. Both charts employ interactive multiview, connecting them according to the user interaction and are indicated to visualization of multivariate data.

Figure 4. Dashboard related to cardiovascular response of children to microgravity simulation. (a) Gapminder chart; (b) Pixel-oriented chart.



For the analysis of means and standard deviation, we use box plots charts, a visual way to depict quartiles of data (Figure 5). Boxplots allow us an efficient way to compare groups and view dispersion and spread in data. They also help to highlight outliers.

Figure 5. Boxplots charts related to heart rate (HR), mean blood pressure (MAP), heart period (HPD), and basic impedance (ZO).



This is yet another example of how the data analysis and visualization, applied to health data, can help understand patterns and discover knowledge, especially when it comes to multidimensional data.

1.5 Discussion and Final Comments

In addition to knowing patients' illnesses, it is increasingly important for health professionals to have data that supports population health management. To achieve this, analytical data visualization techniques and tools such as the clinical dashboard can help significantly, facilitating real-time monitoring, with the help of data that goes far beyond ICD-10 and other medical terminologies.

The cases presented in this chapter are not limited to data analysis alone. These research seek to contribute significantly to the overall quality of medical care. Optimizing resource management, identifying health trends, and improving treatment protocols are fundamental goals that, when achieved, will have positive impacts on the quality of care offered to the population.

Data visualization and visual analytics can optimize the comprehension of epidemiology by streamlining the process of insight about different correlated data. When we analyze an image, we activate our perceptual mechanisms to identify patterns and perform segmentation of elements. For improving perception, the searched information must be placed in focus, distinguishing it from the unnecessary information and promoting the understanding of what is shown. In order to do that, designers of visualization systems should consider the mapping of information to a graphical representation in order to facilitate its interpretation by health professionals and to limit the amount of information that users receive, while keeping them "aware" of the total information space, thus reducing cognitive effort.

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2 The Digital Transformation of the Preoperative Assessment Clinic

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Abstract:

The increase in life expectancy has been accompanied by a rise in the number of surgeries performed. The pressure to gain access to these technologies and advances, coupled with the reduction in available hospital beds, poses challenges that need to be balanced. Scientific evidence demonstrates that accelerating post-surgical recovery reduces complications and costs. Recovery can be expedited through a set of measures that, fundamentally, aim to reduce the stress associated with surgery. The goal of an anesthesia information management system is to monitor the patient's progress throughout the entire perioperative process, from the surgical consultation to hospital discharge. Digital platforms for health data storage have been a reality worldwide for decades, and the digital transformation of preoperative assessment has numerous applications to enhance processes, reduce costs, and improve quality, safety, and satisfaction for surgical patients.

Keywords: preoperative, digital transformation, anesthesiology, screening.

2.1 Introduction

The advent of mobile devices has revolutionized the way we handle data input in our daily lives. Smartphones and tablets have brought agility and multiplied the possibilities of using digital tools that are connected and mobile in the healthcare field. This has given momentum to the Bring Your Own Device (BYOD) movement, taking data portability to another level but also presenting significant challenges regarding data security.

In Brazil, market studies show that 86% of anesthesiologists bring their tablets into the operating room, but only 2% use them for data integration and recording of the anesthetic procedure. They are more commonly used for therapeutic information consultation. The purpose is to leverage the use of this tool already in the hands of the anesthesiologist, connected and within the operating room. Through an interactive and intuitive application, they can access preoperative assessment data, document the anesthetic procedure, and provide real-time safety insights analyzed by algorithms applied to cloud data.

Thus, preoperative assessment is the initial and crucial stage for obtaining information about the surgical treatment process for certain conditions. Identifying risk-imposing conditions and optimizing patients' clinical conditions preoperatively reduce postoperative morbidity and mortality.

At Santa Casa de Porto Alegre, the high demand for the service, the confirmation that most patients treated do not have comorbidities or have mild underlying diseases, and the observation that patients travel considerable distances for their assessments, coupled with the conveniences provided by information technology, lead to the need for research and modifications capable of triaging which patients require in-person evaluation and which can be assessed remotely or, soon, with a degree of automation through machine learning.

Additionally, there is a need to incorporate a point-of-care information system and new technologies into in-person assessments (ultrasound, biological marker assays, among others) to optimize the clinical condition and timely clearance for surgery, avoiding cancellations and delays in preparation, and maximizing the patient's clinical condition. In this chapter, we will present some important aspects of the digital transformation of the clinical assessment of the surgical patient.

2.2 Development

Approximately two-thirds of surgical patients do not present comorbidities or have mild underlying diseases without clinical repercussions. This patient group does not require in-person clinical assessment and should be evaluated virtually, receiving guidance on the importance of physical activity, dietary care, correct medication usage, fasting duration, smoking cessation, abstaining from alcohol consumption, necessary documentation for the procedure, and existing norms and regulations, such as the requirement for a companion in outpatient surgeries.

On the other hand, it is known that approximately 10% of surgical patients have multiple comorbidities and undergo major surgeries. This group represents a higher-risk category and is responsible for 80% of the hospital costs associated with surgical patients. Therefore, a more detailed in-person assessment is crucial for this patient group, specifically evaluating the cardiovascular and respiratory systems in detail, capable of recognizing patterns and identifying associations with postoperative outcomes. Additionally, digitized assessments and obtained images must be available for the anesthesiologist's evaluation before the commencement of anesthesia.

Despite this knowledge being universal, there is a lack of targeted care pathways for these two main segments, and patients are subjected to the same standardized assessment protocol, which is unnecessary for the vast majority and insufficient for patients classified as high-risk.

2.2.1 First Stage: Screening

From a medical perspective, in the initial stage, the digitization of preoperative assessment and the use of AI need to conduct screening to identify which patients require in-person medical evaluation and which can be accessed remotely. This initial requirement must be continuously informed by surgical outcomes to achieve the highest possible sensitivity and specificity across different surgical specialties and types of surgeries. Consequently, the information system should integrate all stages of the perioperative process.

During the initial screening, additional complementary assessments should be conducted for all patients, including risk assessment for nutritional status, the presence or absence of anemia, evaluation of biological markers, risk assessment for delirium, and, utilizing literature-

validated risk calculators, the stratification of surgical risk. Considering these as markers for increased morbidity and mortality and recognizing that the treatment window occurs before surgery, it is crucial that this assessment facilitates timely treatment for issue resolution. Identifying risk-imposing conditions and resolving them reduce postoperative morbidity and mortality. In other words, patients designated for in-person evaluation, while awaiting the consultation appointment, can already initiate the resolution or improvement of their baseline clinical condition.

Table 1. Lists some clinical conditions that should be evaluated and corrected before surgery.

Risk Indicator / Marker	Tools
Nutritional risk assessment #	Validated questionnaires.
Anemia assessment ##	Complete blood count.
Delirium *	Validated questionnaires.
Biomarkers **	
Others	

Approximately 50% of patients undergoing major surgeries are at nutritional risk.

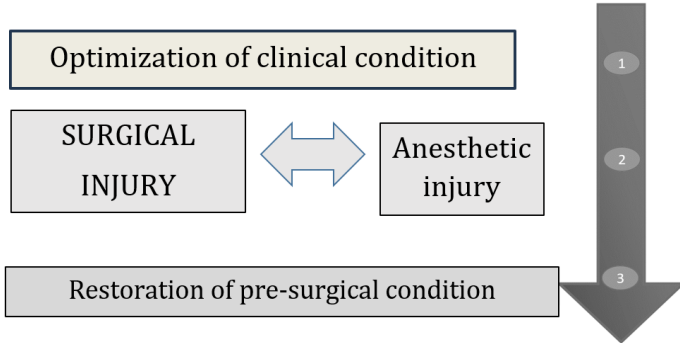
WHO data demonstrates that 30% of surgical patients have anemia.

* Highly prevalent and with prognostic significance in the elderly population, its presence is associated with increased mortality.

** Inflammatory response markers related to worse prognosis in oncology patients.

Digitally documented anesthesia records, composing a cloud-based data repository with OLAP (Online Analytical Processing) database, can be continuously analyzed to provide results to various hospital areas: pharmacy, quality, billing, and protocols commissions such as ERAS, among others. However, collecting and storing data alone is insufficient; it is necessary to transform this information into knowledge through analysis, interpretation, and, primarily, innovation; bringing a new perspective and a new way of acting based on easily accessible and digested information. University departments such as medicine, nursing, pharmacy, engineering, information technology, postgraduate programs, and specific areas like quality, statistics, hospital management, process improvement, among others, will have the opportunity to engage in projects aiming to extract new insights and action plans from perioperative data to enhance the quality, comfort, and safety of patients and professionals. While this text focuses on the digital transformation of preoperative assessment, it is essential to understand that we are dealing with a continuous process represented in the figure.

Figure 1. Perioperative Process. The patient's clinical condition must be optimized for them to undergo surgery and anesthesia successfully. The goal should be to restore the condition to its pre-procedural state or even improve it. The arrow indicates the perioperative process, which should be understood as a continuous care pathway. 1- Preoperative; 2 - Intraoperative; 3 - Postoperative.



2.2.2 Second Stage: In-Person Assessment – Point of Care Evaluation

Perhaps the most essential aspect of a physician's role is their ability to diagnose accurately because without precise diagnosis, effective treatment is compromised, and harm to the patient may occur. There are several necessary steps before a patient enters the operating room, including taking a medical history, conducting a physical examination, preoperative assessment, optimizing clinical condition, obtaining informed consent, administrative documentation, laboratory tests, planning, and providing necessary supplies. Considering that patients move through the system faster than paperwork, the likelihood of all documentation, physicians, and patients arriving on time at the appropriate location is low. The most common cause of delay is the lack of necessary documentation. Moreover, many documents contain the same information, and patients perceive the system's inefficiency as they respond to the same question about five times.

Point-of-care ultrasound refers to the use of bedside ultrasound for diagnostic and therapeutic purposes. Point-of-care ultrasound (POCUS) has been identified as the fastest-growing sector in medical ultrasound imaging. Portability, ease of use, and minimal training are some of the advantages of POCUS. The ability to obtain a rapid result and the convenience of using

it at the bedside are increasing the demand for POCUS.

All images are acquired and interpreted in real time and the information is used for diagnosis and directing therapies. While comprehensive images can be acquired and interpreted at the point of care, the term point-of-care ultrasound usually refers to a simple, quick, and goal-oriented ultrasound examination. It is a tool most frequently used to provide answers to acute clinical questions with a "yes or no" response. However, it can be more sophisticated depending on the professional's qualifications.

POCUS has undergone dramatic innovation in recent years. Indeed, over the last decade, these devices have become more compact, with improved image quality and lower costs, resulting in an expanded role in perioperative assessment and optimization of patients' clinical condition. Additionally, a growing amount of recent clinical research has demonstrated that ultrasound has lower costs and higher diagnostic sensitivity and specificity compared to other initial bedside assessment tools. For example, cardiac POCUS was superior to the electrocardiogram (ECG) for evaluating non-ST-segment elevation chest pain and chest auscultation in identifying selective bronchial intubation. POCUS was also more accurate and faster than chest auscultation or chest X-ray for detecting pneumothorax, pleural effusions, and lung consolidation in intensive care settings. With increasing awareness and evidence supporting the usefulness of POCUS in bedside patient assessment, there is strong pressure for the implementation of POCUS in the curriculum and training of anesthesiology residents. The digitization of in-person assessment, combined with data obtained during virtual screening and images, should be analyzed by AI in search of patterns. Preoperative assessment data, associated with data related to trans and postoperative management, should be compared with the outcomes obtained.

2.2.3 Third Stage: Digital Records and the Patient's Journey

As seen, digital records should accompany the entire journey of the surgical patient and provide data to support healthcare and administrative decision-making, scientific research, insight, and feedback for the implementation of new improvements, and identify opportunities. Indeed, a large amount of data is created during the application of these routines. It is crucial that they are stored, tracked, analyzed, and understood. The assessment conducted needs to incorporate the most modern administrative, clinical, and technological techniques to ensure greater

comfort and safety for patients and greater logistical and economic efficiency. Thus, digital transformation and proposed innovations in the workflow aim for a productive, modern, functional, safe, and especially effective surgical center for people's surgical problems. Patients directly benefit from an infrastructure designed and offered with a focus on excellence.

2.2.4 Fourth Stage: Decision Support

As technology advanced, particularly with the development of more sophisticated algorithms, AI in anesthesiology began to evolve rapidly. Today, we have intelligent systems capable of predicting hypotension in advance during a surgical procedure using cerebral hemodynamic monitoring that improves intra and postoperative patient prognosis, avoiding or limiting the development of cognitive dysfunctions. Preoperative assessments and the cross-referencing of clinical and laboratory data can support decision-making or alert to the existence of certain risk markers and facilitate the choice of more assertive decisions. Considering their value, this information should be available to patients and their families.

To extract genuine value from data, it must be accurate and relevant to the objectives. The process of collecting, extracting, formatting, and analyzing information was once quite complicated, mainly due to dispersion and reliability issues.

Today, however, the development and accessibility of business intelligence software are capable of empowering users, even those without technical knowledge of technologies. This is done through dashboards that present graphs and indicators in a very visual and intuitive manner. With these developments, data science has evolved immensely, becoming a discipline where information technology skills and statistics meet corporate needs, providing means for more quantitative analyses rather than just qualitative ones. Quantitative data analysis focuses on numbers and statistics—the median, standard deviation, and other mathematical models. This type of calculation is based on formulas rather than observations. On the other hand, qualitative analysis focuses on information not defined by numbers or metrics, such as interviews, videos, and impressions. It is based on what people think about something.

2.2.5 Fifth Stage: Data Management and Research

Digital platforms for storing health data have been a reality worldwide for decades. In Brazil, their use and characteristics are defined by the Federal Medical Council (Conselho Federal de Medicina - CFM) through Resolution CFM 1639/2002, which determines "Technical Standards for the Use of Computerized Systems for the Storage and Handling of Medical Records." It addresses the storage time of medical records, establishes criteria for the certification of medical record systems, and provides other provisions, including compliance with the General Data Protection Law. The storage of data, which is now based on Machine Learning, analyzes large datasets, aiding in risk prevention and complication prevention, contributing to a macro evaluation of local health and more accurate individual assessment. Individual data storage also contributes to better segmentation since access is quick and secure. Moreover, it can lead to savings in expenses generated by exams, as they are generally recorded in the patient's file. Ease of evaluation can start from the scheduling process, which can be online, through applications, chats, among others, which also makes the process easier and reduces waiting time. Some platforms even have an online agenda where the patient has the autonomy to reschedule their appointment, if necessary.

These platforms can also be used for online education by offering training resources for patients such as educational videos on what a preoperative assessment is, what it is for, and the benefits of being performed before the surgical procedure. Video and written guidance that advises on the use of medications and fasting, including through more individualized reminders according to comorbidities and the time of the surgical procedure. Illustrations of how to organize your personal belongings to be taken on the day of surgery and videos to demonstrate the patient's entire journey from entering the hospital, such as reception, arrival in the surgical suite, entry into the operating room, the recovery, the waiting room for companions and the moment of discharge, what to do in the event of an incident. The objective is to make the surgical process more transparent and improve patient and family satisfaction. Because being treated with dignity, respect, kindness, accessibility and courtesy is a fundamental interpersonal behavior that increases satisfaction.

Another relevant aspect associated with the digitalization of preoperative assessment is the saving of time spent traveling patients with difficult access to the care location. Considering that Santa Casa serves

patients from hundreds of municipalities in Brazil and that they need to miss a day of work to perform the APO. If we take into account the time saved with assessments that can be carried out virtually, we would have significant savings in terms of assessment hours worked, which could be directed towards more detailed assessment of high-risk patients. This savings extends to municipalities and relieves burdens on the healthcare system.

2.3 Challenges

In Brazil, there are more smartphones than people, and internet access is still a challenge. The gaps range from the quality and speed of the connection to the diversity of devices available for carrying out activities on the internet and the digital literacy of users. Offering training resources for users, user-friendly and intuitive platforms, both for health professionals and for patients and their support network is fundamental. In addition, having the support of other healthcare establishments that can facilitate user access to the app and/or any online consultations is a necessity, especially in remote municipalities where access to the internet network is more limited. It is not uncommon for surgical centers to be without an open or regulated network, or for others to have serious signal and electrical interference problems. A survey is needed and specific improvements made if necessary. Even so, the solution adopted must be robust and modern enough to be able to organize the data on the device in an offline state and synchronize it with the cloud as soon as a connection is possible. The organization of data packets and the technology used are essential for this feature to work properly.

Having good cyber security is another important point. It is necessary to ensure that all digital systems are protected, the information on these platforms is confidential and even with data protection laws, the systems are still flawed and leave patients and healthcare professionals exposed. Digital certification is the goal of platform certification. With digital certification, in addition to the possibility of storing documents only in electronic form - which is cheaper and environmentally friendly - improvements are made in the tax field, and an important contribution is made to document security, since the certification key is encrypted.

There is a need to collect continuous feedback from patients, family members, caregivers and managers, as well as the health professionals

involved in care, in order to constantly improve digital processes, ensuring updating, innovation, satisfaction and quality.

The development and adoption of new technologies depends on a people-focused process. In order to minimize losses due to inadequate records of anesthetic evaluation and other interconnected processes, it is necessary to train the operational team, especially when we consider that hospital turnover is high and that medical professionals can be resistant to change, as they may find it difficult to visualize the associated benefits.

Cultural change is a major challenge and requires challenging and sometimes contradictory skills from the professionals involved. So resilience, flexibility and agility form a curious set of skills, which have proved to be in high demand. The experience of both the patient and the professionals who use the system, as well as the gain for the institutions involved, may be a great facilitator and a driving force towards change.

2.4 Conclusion

Digital transformation can significantly improve the accessibility and quality of preoperative care, as well as provide a more integrated and convenient experience for patients. The operation of the operating room as a whole is becoming increasingly complex. The incorporation of more modern administrative and clinical techniques, such as digital preoperative assessment, which aims to ensure greater comfort and safety for patients and healthcare professionals and greater logistical and economic efficiency, need to be continually practiced, analyzed, and reviewed.

2.5 Conflicts of Interest

The authors declare no conflict of interest related to this chapter.

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3 Digital Health and Black People's Equity: Technology Implementation to Health Promotion

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Abstract:

Due to structural racism and their history of enslavement, Black people appear as one of the most vulnerable socioeconomic groups in Brazil, being disproportionately affected by several health issues in comparison to their white counterparts, contributing to health inequalities. Digital health can improve health equity, but, due to digital divide, there is a need to stimulate effective approaches that will not exacerbate health disparities. To promote Black people's health through Digital Health, we present a few strategies and characteristics that have the potential to address equity.

Keywords: Digital Health; Black Population; Equity; Digital Divide; Representativeness.

Sustainable Development Goals (DSG): 3. Good Health and Well-being; 10. Reduced Inequalities.

3.1 Introduction

Digital health has been the focus in recent years on planning and implementing public health policies. With the COVID-19 pandemic scenario, there was an acceleration in health computerization processes, resulting in solutions such as telemedicine and electronic medical records (EMR) supported by data cloud, which allowed care for the population remotely, protecting the health of patients and healthcare professionals, in addition to allowing the tracking and monitoring of infected patients.

The use of information technologies to facilitate human functions is nothing new in modern times. In the health area, it is easy to see that the use of technologies has always been present, with their mastery being essential in helping health managers in the formulation and monitoring of public policies [LISBÔA; CAETANO, 2020]. It was between the 1970s and 1990s that the first modular IT systems were used, in a period known as Health 1.0 [MACEDO; MARTINS; TOURINHO, 2022], paving the way for the increasing use of computerized systems in healthcare practices and the formulation of the “digital health” concept. Today, we currently find ourselves in the phase called Health 4.0, which encompasses technologies such as the Internet of Things (IoT), Artificial Intelligence (AI), and Blockchain. [MACEDO; MARTINS; TOURINHO, 2022], also known as 4.0 industry technology tools [VENTURINI; PINTO; OLIVEIRA NETO, 2021].

This acceleration of computerization processes, however, raises a question: to what extent the use of computerized algorithms and standardizations would not be contributing to an increase in health inequities, especially in countries that present very significant social inequalities that translate into levels of access to very differentiated health systems and where digital divide is quite significant [GROSSI; DA COSTA; DOS SANTOS, 2013] It is well known that health solutions, when implemented without addressing equity, have the potential to either reduce or exacerbate inequalities, in addition to creating new risk factors for inequity [WERE; SINHA; CATALANI, 2019], being race a social determinant of health responsible for a major factor of inequity [O'NEILL et al., 2014].

In Brazil, a segment of the population that has poor access to healthcare systems and shows the worst health incomes is the Black population [BRASIL, 2016], as a result of the country's history of slavery that resulted in structural racism [ALMEIDA, 2019]. According to data from the Institute for Applied Economic Research [IPEA], in 2011, only 26.3% of Black Brazilian women had medium or high-income levels, in addition to

residing in regions with less running water, less sanitation, less regular collection of garbage, less access to food, school, health services [FIOCRUZ]. Diseases that prominently affect this population are sickle cell disease, type II diabetes, high blood pressure, and glucose-6-phosphate dehydrogenase deficiency [BRASIL, 2017].

This background led to the establishment of the National Policy for Comprehensive Health of the Black Population (PNSIPN), in 2009, to promote equity in health for the Black population, especially combating institutional racism in the Unified Health System (SUS) [BRASIL, 2017]. Despite having the second largest Black population in the world and having indicators that place this population as one of those with the worst health conditions (BRASIL, 2019), this policy only emerged in the 2000s, in a period of intense struggle by social movements. With this policy, the Ministry of Health finally recognizes the need to confront institutional racism, overcoming the barriers that negatively impact the health indicators of the Black population [BRASIL, 2017].

Regarding internet access, Black women in Brazil uses the internet to a much lesser extent to access public services and educational websites [CETIC, 2021], demonstrating that, more than a question of access to technologies, we have a problem of digital literacy, transcending a purely economic issue. In a digital divide study carried out in the United States, Mitchell et al (2019) found that, among the elderly population surveyed, participants considered Black and Hispanic use technology much lower than whites. According to Gergeren Barnett et al (2022), despite the obvious potential for increasing health care through digital technologies, it alone is not enough to reduce health inequities without a significant change in public health policies, mainly due to still low rates of inclusion and digital literacy among disadvantaged populations.

Given this background, for digital health solutions to focus on equity, it is imperative being planned and implemented with characteristics and specificities that seek to mitigate these inequalities. Therefore, some technologies that are part of the Health 4.0 scenario are presented here and proposed ways in which they can be implemented with characteristics that promote Black population's health. These proposals were prepared to take into account the results of a scoping review carried out in 2023, with the aim to select studies that focus on promoting the health of the Black population through digital health solutions.

3.2 Electronic Health Records

Electronic Health Records (EHR), according to WHO, is generally defined as a longitudinal data record with entries provided by health professionals and services when providing health care [WORLD HEALTH ORGANIZATION, 2006]. The implementation of electronic health record is present in Brazil's current Digital Health Strategy, being essential for the National Health Data Network (RNDS), allowing the health systems interoperability and access to patient data throughout the territory [BRASIL, 2020].

Without doubt, electronic health records, especially with the recording of disaggregated data, are essential for defining public policies for specific populations. However, there are still many difficulties in obtaining and using this data in health services [CRUZ, 2021]. In fact, the electronic health record reflects the vision of the people who created it. Thus, reflecting structures and elements of their point of view. EHR are perceived as one of the main digital health tools for monitoring and consequently developing public policies for the black population, and its improvement is essential. For Cruz (2021), a proposal for the use of health records with focus on equity is in an interprofessional and person-centered manner, in collaboration with the social control of the linked territory. Furthermore, it is necessary to include records on “experiences of discrimination” in the data, allowing diagnoses that take into account the risk of compromised human dignity.

3.3 Telemedicine

Telemedicine is understood as a digital health solution in which interaction between patient and healthcare professional is carried out remotely, whether by telephone or video, a modality widely used during the COVID-19 pandemic, being a interaction between a client at one end who receives care from a healthcare professional from a remote location at the other end [CRAIG; PATTERSON, 2005]. Telemedicine can provide access to quality healthcare where there are not enough health posts or professionals [ASI; WILLIAMS, 2018]. According to Stein et al (2020), increasing patient accessibility to telemedicine solutions can allow patients to seek medical care more quickly, better adhere to prescribed treatments, and promote the quality of life of patients with chronic diseases.

In Brazil, there is a greater use of telemedicine among private hospitals and clinics, with very little use by public health services

[SCHEFFER et al., 2022]. Considering that the majority of public patients in Brazil are Blacks, there is a concern about the effectiveness of this technology and, therefore, the need to develop strategies to mitigate this inequality. For telemedicine can promote Black people's health, some actions must be addressed: a first aspect concerns the importance of developing solutions with community participation [ELK et al., 2020; LYLES et al., 2022] and adaptation, especially with regard to culture in solutions [STEWART et al., 2021], meeting an appreciation and empowerment of patient, especially with regard to valuing blackness within a public health context [STEWART et al., 2021].

One can see an alignment of these measures with the PNSIPN guidelines, such as the development of information, communication, and education processes, which deconstruct stigmas and prejudices, in addition to strengthening a positive Black identity that contributes to reducing inequalities [BRASIL, 2017]. Furthermore, the importance of religion must be highlighted [ELK et al., 2020; STEWART et al., 2021], given the importance of valuing religions of African origin for the Black population in the Brazilian context, being this is an urgent issue given the various prejudices that still exist and violations that it suffers [AKOTIRENE, 2020].

3.4 Big Data Cloud

The use of Big Data Cloud is one of the typical innovations of the Digital Health 4.0 [REIS; GONÇALVES, 2018]. Big Data refers to the accumulation of different data sources and informational patterns that can be computed to promote better decision-making both in patient care and in the management of health systems [MACEDO; MARTINS; TOURINHO, 2022]. The data cloud provide the broadband infrastructure for storing this large amount of data. Systems based on cloud storage allow the development of online applications, being a cost-effective digital health method (ASI; WILLIAMS, 2018). Through the combination of Big Data with cloud storage, the healthcare manager can identify areas for improvement and allow people to make more informed decisions, helping to move the entire healthcare sector forward (MACEDO; MARTINS; TOURINHO, 2022).

For this technology to promote equity, however, research in this area must include the community as the main actor in decision-making [TAYLOR et al., 2018]. Community empowerment is not only essential for the engagement of the population involved but also enrich researchers involved in exchanging knowledge and experiences with marginalized communities,

allowing them to deconstruct prejudices and develop more creative solutions, which meet the specific needs of populations. This type of construct is in line with what is observed in the guidelines of the PNSIPN, which relate respectively to encouraging scientific and technological production in the health of the Black population and the development of information and communication processes that deconstruct stigmas and prejudices, as well as the objectives of the law, which concern the inclusion of the specific demands of the Black population in health promotion processes, in addition to promoting studies and research on racism and the health of the Black population [BRASIL, 2017].

3.5 Artificial Intelligence

Artificial intelligence (AI), can be understood as the field of science that investigates how computers can learn from experiences and understand the world in terms of a hierarchy of concepts, with each concept defined through its relationship to simple concepts [STEIN et al., 2020]. In healthcare, the use of AI is being applied in fields such as clinical research, decision support and specialized therapies [RAZA; VENKATESH; KVEDAR, 2023]. One of the biggest challenges that arise from the use of AI is the elimination of biases, especially racial and ethnicity bias, since the majority of image banks and data that feed this technology come from Europe or the United States, with a very Eurocentric worldview. Furthermore, AI algorithms are created by people within the confines of structural inequalities, so bias can be enmeshed in the decisions made by the developers of these solutions [RAZA; VENKATESH; KVEDAR, 2023].

The use of AI to build digital health algorithms can mask prejudices under the guise of “machine rationality”. Being created by human beings, it ends up reproducing social structures such as racism, especially in societies like Brazil, which still suffer the consequences of the constructed myth of racial democracy. The 2018 Gender Shades study cross-sectionally evaluated race and gender biases in 3 commercial facial recognition algorithms (BUOLAMWINI, 2018). This study demonstrated much greater accuracy in recognizing white men's faces (0.8% error) and the group made up of Black women's faces had a higher incidence of recognition errors (34.7%). According to the authors, this is mainly due to a greater concentration in the databases that feed the AI of white men, something around 80% of the representations, in addition to the digital camera

settings themselves, which are calibrated to better expose white skin faces (BUOLAMWINI, 2018).

There is an urgent need to combat this type of bias. In many cases, it is not necessary to change the way data is collected to feed AI, but rather the way this data is labeled and used to build algorithms. For this, data collection and categorization carried out with community support is essential. Furthermore, there is an urgent need for representativeness policies for the construction of databases, the need for “racial literacy” in machine learning, and the discussion about possible racial limitations in the choice of data for developing algorithms. That is why diversity of the teams that feed these databases and build algorithms is also necessary, reinforcing the importance of affirmative policies.

3.6 Web-based interventions

Web-based interventions refer to solutions that use digital platforms to promote health. An example is the provision of health information on websites. This information can be made available in the form of texts, videos, courses, or games, allowing the patient to self-learn. According to Sherman et al (2021), network-based health resources promote an optimized path to disseminate health information by their immediacy, accessibility at any time of the day, and the potential for constant update of information and reach, being crucial for the development of health literacy. For Ramos and Chavira (2019), interventions delivered via computers with internet access have proven effective for a variety of disorders such as body dissatisfaction, sexual dysfunction, disordered substance use, eating disorders, bipolarity, and schizophrenia, among many others. In the United States, there is a growing of search for health information online by the Black population, especially young people, compared to other racial groups (LITTLEFIELD; EDWARDS; AKERS, 2014).

As with other technologies, for their effectiveness, there is a need to place the community at the center of the development of these solutions (CULLEN; THOMPSON; CHEN, 2017; JONASSAINT et al., 2017; LITTLEFIELD; EDWARDS; AKERS, 2014), thus producing patient-focused solutions, reflecting their experiences and reality (CULLEN; THOMPSON; CHEN, 2017; VILARO et al., 2020) and with high cultural adaptation (JONASSAINT et al., 2017; JOSEPH et al., 2015). Furthermore, the importance of representation in digital health solutions aimed at the Black population is highlighted (CULLEN; THOMPSON; CHEN, 2017; SHERMAN et al., 2021; VILARO et al.,

2020). One way to achieve this is a website design with Black representations (LITTLEFIELD; EDWARDS; AKERS, 2014), in addition to the preference for virtual assistants with Black characteristics (VILARO et al., 2020).

3.7 MHealth

MHealth concerns services and information provided through mobile devices, such as cell phones and handheld computers. [WHO, 2012]. For Thomas Craig et al (2020), mHealth is characterized by the use of technologies that enable mobile devices to send and receive health messages, and use spatial positioning systems, among other applications. Furthermore, mobile devices can be used to gather clinical data and promote healthcare by employing interventions such as email, and multimedia solutions, combined with internet access [RAMOS; CHAVIRA, 2019].

MHealth had a rapid rise, especially in developing countries, due to the high penetration of mobile devices and the absence of other modern healthcare infrastructures [WHO, 2012]. It is also worth highlighting the popularization of smartphone applications, which today exist in the most varied types and for the most diverse functions [RAMOS; CHAVIRA, 2019], in addition to being low-cost solutions, compared to other. In the United States, the Black population is the group that owns the most cell phones, accounting for 87% of the population compared to 80% of the white population [JOSEPH et al., 2015]. Furthermore, it was found that Black and Latin are more likely to search for health information using their smartphones [JACKSON; SEHGAL; BAUR, 2022]. In Brazil, there is equality about internet use between Blacks and whites. However, when it comes to the exclusive use of cell phones to access the internet, the Black population remains in the lead [CETIC, 2021], which demonstrates the potential of this technology to promote health for this population.

Among the main contributions found in mHealth studies for the implementation of effective digital solutions to promote Black people's health, there is a great concern with the design of such applications. A preference was observed for intuitive and easy-to-use applications [CHANDLER et al., 2020; MCCALL et al., 2021, 2022], with limited notifications [MCCALL et al., 2022], a Black patient-centered design [DAVIDSON et al., 2015] and the preference for audiovisual materials instead of texts [CHANDLER et al., 2020; HEINEY et al., 2020]. Also, there

is a great concern about the development of digital literacy [DAVIDSON et al., 2015; HEINEY et al., 2020; JACKSON; SEHGAL; BAUR, 2022; NUNDY et al., 2013], considering that cell phones are used by a wide variety of users who have the most diverse levels of literacy.

Similar to other digital solutions, several studies advocate the need for cultural adaptation of the developed application (CYRIAC et al., 2021; DAVIDSON et al., 2015; HEINEY et al., 2020; JACKSON; SEHGAL; BAUR, 2022; STEINBERG et al., 2013, 2017), as well as the importance of placing the target group as a protagonist in the development of the solution, whether as the main actor (CHANDLER et al., 2020; EGEDE et al., 2017; JACKSON; SEHGAL; BAUR, 2022) or in collaboration with other actors involved (CYRIAC et al., 2021; SHERMAN; GRANDE, 2019) such as health professionals, academia and developers of software, in addition to the importance of representation, whether in the design of the application (CHANDLER et al., 2020), or in the dissemination of geographic location of Black professionals (CHANDLER et al., 2020; MCCALL et al., 2021, 2022).

Finally, the use of mHealth applications appears to have great potential to act as social support (EGEDE et al., 2017), whether through community support networks (CHANDLER et al., 2020) chat groups or publicizing events about Black people's health (MCCALL et al., 2022), thus providing an exchange of experiences between different users (CYRIAC et al., 2021), generating a sense of community (NUNDY et al., 2013), in line with the PNSIPN recommends (BRASIL, 2017).

3.8 Conclusion

In this chapter, several characteristics, strategies, and precautions were proposed that, if taken into consideration, have the potential to address equity in the development of digital health to promote Black people's health. It is important to highlight that much of what was discussed here focuses mainly on the digital solutions analyzed, often not addressing structuring issues such as internet availability or access to electricity and digital devices in a given location, for example. In other words, the external factors that greatly influence social determinants of health, such as place of residence or access to education, factors aggravated by racism and that can influence the success or failure of many of the solutions, impacting issues such as digital and health literacy, as well as digital exclusion. This factor calls into question whether these digital solutions have the potential to combat health inequities, given that

attacking social determinants is fundamental to public equity policies, reducing practices to individual initiatives. I believe that this question is not completely correct, considering that among the findings in this study, several have characteristics that address issues such as digital literacy, racial literacy, and the valorization of blackness through representation and the construction of support networks meeting what the PNSIPN foresees.

We can highlight some fundamental characteristics, which encompass all types of digital health technologies. First, is the importance of placing the community, in other words, the target population of the solutions, as the main actor in the development of equity policies (CULLEN; THOMPSON; CHEN, 2017; EGEDE et al., 2017; ELK et al., 2020; JACKSON; SEHGAL; BAUR, 2022; JONASSAINT et al., 2017; TAYLOR et al., 2018; VILARO et al., 2020). There is no need to talk about promoting effective public policies without listening to the demands of the populations addressed, through their voices. This is even more important when dealing with a population that “has no voice” within a racist society. As Kilomba (2019, p. 74) reminds us, in order to get closer to the lived reality of racism, a change of perspective is necessary. The author classifies this change as the transformation of an object into a subject, emphasizing that this transformation should not be understood as a privilege, but as an extremely necessary concept (KILOMBA, 2019). Ribeiro (2019, p. 12), says that there is a need to remove Black people from invisibility in order to think in solutions for structural racism. The most effective solutions showed in literature are precisely those created either by the community or jointly with the other actors involved, combating digital exclusion in this way (LYLES et al., 2022).

Therefore, qualitative research with a focus on reducing inequities becomes important (JONASSAINT et al., 2017). There is no point in sophisticated technology solutions if they do not satisfy the needs and be appropriate to the context and literacy levels of the populations involved. With this in mind, focus groups (MCCALL et al., 2022), or interviews (CHISOLM; SARKAR, 2015), are more effective in collecting data on the preferences and desires of the target population to improve the usability of solutions.. Furthermore, it is necessary to understand that in academic research racism does not always appear explicitly. Therefore, numbers and statistics often do not reflect historical, political, and cultural factors within vulnerable groups (LOPES, 2005, p. 1599).

A second characteristic presented concerns the need to carry out cultural adaptation in technological solutions (CYRIAC et al., 2021; DAVIDSON et al., 2015; JONASSAINT et al., 2017; JOSEPH et al., 2015; STEWART et al., 2021). Especially when it comes to technologies that favor “self-care” in chronic illnesses, support for the individual’s cultural values and beliefs appears as fundamental. Without a doubt, the valorization of Black culture is one of the pillars of the PNSIPN and extremely important in colonized countries with a past of devaluation and erasure, which also applies to religions of African origin, commonly marginalized (ELK et al., 2020; HEINEY et al., 2020; STEWART et al., 2021). We must be careful, however, about what Fanon already warned about in the context of structural racism, Black culture, even offering possibilities for contesting racism in society, can always be distorted and treated as “exotic” (ALMEIDA, 2019). It is therefore important that we build policies to value Black culture and for this the role, social movements, quilombola movements, and laws is essential.

A third point concerns the importance of incorporating intersectionality in studies on digital health and equity, a concept that is even more sensitive in developing countries, which have high rates of social inequalities and where a large part of vulnerable populations fall into two or more factors of inequities, exacerbating poor access to quality healthcare and digital exclusion. Several studies treat exclusion in an intersectional way between race and gender, addressing the analysis of digital solutions among Black women (CHANDLER et al., 2020; JOSEPH et al., 2015; MCCALL et al., 2021, 2022; STEINBERG et al., 2013, 2017; VILARO et al., 2020). According to Akotirene (2020, p. 62), intersectionality has the power to strengthen anti-racist movements, in addition to feminist movements in defending agendas for Black women. According to the author, the lack of a methodology that addresses racialized marking within feminist theories, making the reality of Black women invisible, is one of those responsible for the high rates of violence against this population (AKOTIRENE, 2020). Within this context, eh have the crucial importance of collecting data in a disaggregated way, establishing the concept of race as fundamental, with digital health having a strategic role (CRUZ, 2021).

Still in the same line, a fourth point is the importance of representativeness, also one of the main premises of the PNSIPN. Public policies such as affirmative action become crucial in the context of overcoming racism, allowing the Black population to feel represented in

positions of power historically reserved for whites (RIBEIRO, 2019). This is demonstrated in several studies when, for example, participants point out the need to access Black health professionals as a possibility of providing more qualified care (CHANDLER et al., 2020; LITTLEFIELD; EDWARDS; AKERS, 2014; MCCALL et al., 2021, 2022) or when arguing for the need for the design of applications to be representative of the Black population (CHANDLER et al., 2020; CULLEN; THOMPSON; CHEN, 2017; ELK et al., 2020; LYLES et al., 2022; VILARO et al., 2020). Furthermore, representation also concerns the appreciation of this culture, developing an appreciation of blackness (CHISOLM; SARKAR, 2015; STEWART et al., 2021). In turn, the racial literacy of health professionals and other actors involved with digital health has an important contribution role that deserves to be addressed (LYLES et al., 2022). Algorithms that use AI demonstrate how the failure of placing racial relations as central in the implementation of digital health solutions has contributed to an increase in health inequities (OBERMEYER et al., 2019).

Finally, a fifth characteristic refers to the creation of support groups or the importance of the notion of “belonging” and how this influences health outcomes, both clinical and usability of solutions, functioning as social support for patients in vulnerability. In several studies, this aspect of the digital solution was considered one of the main factors that contributed to the success or feasibility of the solution (CHANDLER et al., 2020; CYRIAC et al., 2021; EGEDE et al., 2017; MCCALL et al., 2022; NUNDY et al., 2013). This question brings us back to the importance of valuing Black culture in health solutions, and also once again valuing blackness. Centralizing efforts in this sense, we can base ourselves on important teachings such as Ubuntu, an African philosophy originating from the Bantu peoples, which praises the role of the community and tolerance in human existence itself and can contribute greatly to the construction of the concept of democracy itself (DJU; MURARO, 2022).

It is concluded that institutional and structural racism, in addition to affecting various social determinants of health such as place of residence, employment, and educational opportunities, is in itself one of the main social determinants of health in our society. Therefore, digital solutions for this population need to be built with a focus on equity. For this to occur, we present a several characteristics that, if taken into account, have the potential to promote equity in digital health solutions development. In addition, it is extremely necessary to incorporate the race criterion in

scientific research, with the peculiarities that the Black population faces in this scenario. With the creation of the PNSIPN, there is no longer any doubt Black people's health requires differentiated care with appropriate public policies. It is expected that managers, health professionals, and designers of digital health solutions increasingly reflect on how technology is never neutral and ends up reproducing culture and social relations in which it is inserted, including racism.

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4 Data Mining as an Ally in Healthcare

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Abstract:

Health data is constantly generated, in a heterogeneous, irregular, incomplete and abundant manner, making the task of analyzing it in an agile, adequate and complete manner arduous. The use of technological resources, such as information and communication technologies, data mining and artificial intelligence, have brought opportunities for the treatment, management and analysis of information generated by health services, highlighting possibilities for management and individualized care. The fusion of interdisciplinary areas of knowledge, such as health and information technology, has become sustainable and essential, generating a new way of caring, especially in oncology.

Keywords: Data Management; Data Mining; Health Information Management; Oncology Nursing,

Sustainable Development Goals (SDG): 3. Good Health and Well-being.

4.1 Introduction

A high volume of data are generated by health services at all times, which are highly heterogeneous, sometimes irregular or incomplete, making it impossible to use them fully (Fayyad; Piatetsky-Shapiro; Smyth, 1996, Galvão; Marin, 2009; Tarver; Menachemi, 2016) Such data are classified as “big data” and due to their relevance, have brought changes to the traditional way of analyzing health data (Fernandes; Chiavegatto, 2019). Information is present in people's daily lives, mediating their relationships, being crucial for the evolution of society, especially in health, influencing the way of generating resources, well-being and quality of life, being an asset of high value (Araújo *et al.*, 2019).

The manual way of storing health data has been replaced by computerized methodologies, saving time and producing organization and agility in processes. Both private and public institutions are moving towards digitalization, favoring more reliable and better accessible data (Gomes; Silva; Rached, 2019).

Despite all the technological and human resources already existing and applied, it is still possible to envisage new possibilities for solving problems through the incorporation of three axes of technology imputed in the modern area, namely: the axis of information and communication technologies (ICTs), the data mining (DM) axis and the artificial intelligence (AI) axis and its improvement methods (Neto *et al.*, 2020).

Given the above, the objective is to report the use of information technology, through the treatment and management of health information using the data mining technique, an aspect of AI, as an intelligent and assertive way of processing information in the field of health and its management, to better care and management practices. This study meets one of the Sustainable Development Goals in Brazil proposed by the United Nations, more specifically Health and Well-being, to guarantee access to quality healthcare through new scientific knowledge (NUB, 2019).

The topic is current and relevant since the accumulation of data and information through electronic tools is constant and growing, enabling various analyses, whether of the people involved as well as the organizations themselves. The health sector, especially population health management, can benefit from this practice, where correctly organized and treated data can serve as a basis for decision-making or strategic actions within institutions (Araújo *et al.*, 2019).

4.2 Health data: generating valuable information

The management of such complex and distinct elements, such as the translation of healthcare images and texts or administrative records into categories, requires great knowledge and effort from the specialist to classify and group them. Therefore, to make this task more organic and less expensive, techniques can be used to prepare and analyze data automatically, through artificial intelligence (Fernandes; Chiavegatto, 2019). AI allows for better preparation, use and applicability of data, making it one of the most promising technologies in healthcare (Dourado; Aith, 2022).

A major impact on clinical practice is expected through its use, especially through algorithms formulated to work with the human brain, revolutionizing the management of health systems, the relationship between patients, the care chain and also health promotion. In this way, an immense transformation is projected in the structure of health services through digital health, with a consequent improvement in the quality provided and cost reduction, brought mainly by the knowledge that information is one of the main strategic resources that organizations have (Dourado; Aith, 2022).

The appropriate use of information technologies in health data provides tools to help and search for more and better published knowledge, favoring and supporting professionals (Fayyad; Piatetsky-Shapir; Smyth, 1996; Galvão; Marin, 2009; Tarver; Menachemi, 2016). Among the possible strategies for managing such information, in this text, data mining stands out as a protagonist in the use and analysis of health data, as a way of bringing knowledge to the specialist responsible for caring for individuals.

DM in health is one of the ways of using information technology combined with artificial intelligence, a technique that has shown itself to be very promising in using this information more effectively, being a divider in the area of medical research, showing excellent performance when it comes to assessing patient risk, creation of disease prediction models and also as a pillar in clinical decision making. Thus, there is a unique opportunity to use public or private databases containing large-scale medical information, to support health care (Zhu, 2020).

However, it is important to highlight that the use of information technology in the processing of institutions' data, for the most part, is not foreseen in the budget, as well as the costs for allocating the infrastructure necessary for its implementation (Araújo *et al.*, 2019). For this process to

occur, it is necessary to systematically process the growing amount of information generated. In this context, it is expected that information will be integrated through tools based on artificial intelligence, to increase diagnostic accuracy and therapeutic management. One of the obstacles still faced is the complex healthcare environment, which makes it difficult to translate it into data that allows clinical research, requiring systems integration, interoperability standards, appropriate IT infrastructure and team education (Bukowski *et al.*, 2020).

The researchers Bukowski *et al* (2020) also cites the importance of correct data management in the health sector, through the creation, reuse and storage of clinical and research information, with quality assurance, integration and reuse of such data. Thus, some areas of knowledge already make use of computer-assisted support, to facilitate data interpretation, helping humans (Yu; Beam; Kohane, 2018). It is necessary to impose a great effort on the part of infrastructure services in information technology to enable the interoperability of systems, providing a bidirectional process between “bench” and bedside (Bukowski *et al.*, 2020).

4.3 Technologies combined with management

The World Health Organization brings the concept of digital health as the safe and economical use of information and communication technologies, functioning as support for health and adjacent areas, including health care, health surveillance, and health research, among others. It comes with the explicit objective of making systems more efficient, clearly impacting the provision of services in the health sector around the world (WHO, 2023).

Information security and system interoperability are a constant concern and need in the health sector due to the large volume of data generated by operational, administrative and care processes (Araújo *et al.*, 2019). There are several technologies implemented today in services, which range from simple tasks such as an agenda for professionals, electronic medical records or financial management of services that are gradually being replaced by computerized methods. Due to the intense and constant generation of clinical data in the healthcare sector, such as patient records, medical reports, drug purchase and management information, as well as data related to laboratory reports, electronic health records and images, among others, there is an excellent opportunity to analyze such data using current information technologies (Subrahmanya *et al.*, 2022).

Health services, as well as other areas, have invested efforts to improve their management, where, in addition to communication technologies, information technologies have been playing an essential role in the mechanisms of innovation and business progress, transforming how care is provided and also to manage, both in health and user relationship management (André; Ribeiro, 2020). The authors also mention that the use of technologies to support health is an inevitable path to be taken, as it allows sustainable competitiveness (André; Ribeiro, 2020), and is also an essential tool for health care (Silva *et al.*, 2018).

The researchers state that in addition to supporting the provision of health care, the use of technologies has a significant impact concerning economic management, and management of critical, financial and production data (Matos; Nunes, 2018). Thus, data mining stands out again, this time in systems integration, facilitating the obtaining of accurate information in different areas of knowledge, being useful in decision-making, contributing to the interface between sectors and adding high value to the business (Souza; Sena, 2012).

Thus, DM applies efforts to formulate, analyze and implement solution processes that allow, fluidly, the extraction of important and significant knowledge and information from data generated in an unstructured way (Toklu; Prashad, 2020), being the reality of several services, which store heterogeneous data in their databases, by also diverse stakeholders. However, due to the organization of these providers and also concerning privacy and ethics care, as well as data ownership, much of this information-rich data that would be useful currently ends up trapped within the organizational boundaries of clinics, hospitals and individual monitoring resources, not allowing for discoveries using data and information technology for health care (Bukowski *et al.*, 2020).

It is possible to establish a competitive potential when health information is appropriately used, resulting in better customer/patient assistance and also optimizing the entire chain of products and services, thus being a strategic management tool, where it is possible to directly influence the result of organizations from correct use (Schmitt; Brancher; Franzen, 2019).

4.4 Impacting healthcare

Through the identification of hidden patterns and relationships evidenced by DM, correlations of information are brought to light, supporting more assertive and anticipated decision-making by managers and health professionals, based on the extraction of knowledge from the volumes of data generated by health services (Fayyad; Piatetsky-Shapiro; Smyth, 1996, Galvão; Marin, 2009, Tarver; Menachemi, 2016). The researchers still highlight its importance about the identification of more vulnerable groups, since this technique allows knowledge of prevalence and incidence, with the creation of hypotheses for scientific investigation and subsequent intervention focused on care (Dalagassa *et al.*, 2019).

When using this technique, it is possible to stratify computerized data analysis by transforming raw information into tangible and useful information, to contribute to the decision process to make changes, and benefit management (Neto Correia; Marques, 2020). The authors also mention the importance of the quality of the decision-making process for the success of the expected result, a fact that is also positively influenced by the use of information technologies.

Regarding oncology, there are currently a greater number of studies aimed at predicting cancer survival using patient-specific attributes, mainly comprising demographic and medical characteristics, through traditional machine learning techniques, but new ways are being moved towards hybrid approaches to the use of information technologies for decision making (Kaur; Doja; Ahmad, 2022). New studies have emerged using data mining with a focus on recent diagnostic and therapeutic advances, such as the so-called immunotherapy, which highlights management challenges due to the high cost as well as the healthcare team, who need to be able and trained to deal with possible side effects. Such studies bring innovations in favor of care, as they outline the profile of patients most susceptible to occurrences throughout their therapeutic journey, helping professionals with individualized and early care, through DM techniques and machine learning (Chen; Zhang; Wu, 2022; Zhang *et al.*, 2022; Liu *et al.*, 2023).

Because of the above, it is clear that through the analysis of data generated by health services, using information technologies, especially the DM technique, new guiding information can be discovered, which would not be possible otherwise. Through this methodology, as well as the use of cloud storage among others, it is possible to reduce costs, increasing the quality

of healthcare (Subrahmanya *et al.*, 2020).

In short, we can observe that the union of information technology with the health sector has occurred substantially, not only about data storage and its functionality but also its management and interpretation, bringing valuable information to professionals and managers, facilitating and supporting decision-making based on new knowledge identified through technological modalities. Technological innovations permeate the areas of management, health administration and also the care area, allowing professionals to have more subsidies and support for their decisions, providing more individualized and quality care.

4.5 Final considerations

Investments are needed in the field of information technology by health services, in order to improve the storage, manipulation, administration, interpretation and use of the data generated. The interface between the different areas of knowledge, such as medicine, biomedical informatics, and management, among others, is urgent so that the information generated can be used in a more assertive way in health, bringing resources to decision-makers as well as the team that provides care, positively impacting the entire care chain, including the patient. To expand and deepen knowledge through data mining about local information, one must think about the interoperability of systems, to access them for the benefit of society. The field of oncology, in particular, has enormous potential to benefit from such a fusion, as it is constantly evolving both diagnostically and therapeutically, with alarming numbers of new cases, but with underutilized data, preventing the discovery of new knowledge based on local clinical and epidemiological data.

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5 Challenges in Extracting and Interpreting Healthcare and Administrative Data for Long-Term Studies

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Abstract:

Extracting and interpreting health data that are available on digital platforms presents challenges beyond those inherent of general information systems. Information systems and the organization of the data they contain are constantly changing, requiring continuous improvements in data analysis. Health information systems introduce added complexities and challenges related to data acquisition and quality, the diversity of healthcare specialties and their specificities, legal and ethical issues, and other factors that impact these systems. Furthermore, as the amount of data stored continues to increase, the time factor presents even greater challenges. To maintain the meaning of the data over time, data governance policies are essential, particularly in environments with increasingly integrated information systems, such as the healthcare industry.

Keywords: Electronic Health Records; Health Information Interoperability; Information Sources; Data Collection; Metadata.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure; 16. Peace, Justice and Strong Institutions; 17. Partnerships for the Goals.

5.1 Health data

From the time of Hippocratic medicine to the present, clinical observation has been essential for understanding patients and the factors associated with their diseases [Gusmão 2003; Brener and Lichtenstein 2022]. With the evolution and specialization of medical knowledge since the 18th century, observations have become progressively specialized and specific [CREMERS-SP 2013], which is presently identified as data. Until the mid-1960s, professionals likely relied on oral presentations (conferences, lectures etc.) and written documents (books, articles, records, medical histories, prescriptions etc.) as the primary means of sharing healthcare data. Often, these data were only available within the physical archives of the responsible professionals and hospitals. Storing and retrieving physical data, especially when dealing with a large amount of information, is a challenging task, limiting its use for purposes such as data analysis for knowledge construction [Greene et al. 2019].

Promising digitization initiatives were already underway with IBM mainframes towards the end of the 1950s, revolutionizing data retrieval processes, previously measured in "man/month", to "machine/minute" [Greene et al. 2019]. This gradual expansion of the digitization of hospital data, which was later known as Electronic Health Records (EHR), gained momentum in the late 1960s with the emergence of computer networks [Lino and Martins 2021]. Arpanet, the precursor to the modern internet, was invented during this period, and these networks became increasingly popular in the 1990s. This trend expanded to microcomputers as well [Machado 2009]. These events and concepts provide context for current data access. Information systems enable the request, extraction, and interpretation of data, even from institutions that are physically inaccessible. However, the ease and diversity of data access present challenges for researchers, health technology professionals, and health managers seeking to utilize this information. Such challenges must be confronted in order to maximize the potential benefits of this data. What are these challenges? This chapter outlines several key challenges from a general perspective and in the realm of healthcare, as well as supplementary obstacles for long-term research.

5.2 General data extraction and interpretation challenges

Datasets that are shared are typically accompanied by a data dictionary or metadata; these dictionaries are even more important when dealing with digital data. This document provides a description of the semantic purpose of each type of data, including information about its origin whenever applicable [Da Silva 2023]. The completeness and presence of metadata are crucial for interpreting data, as the absence of it may render the obtained dataset unusable. By providing context for the origin and purpose of a particular dataset, the data dictionary facilitates the identification of other datasets with similar objectives.

Similar or redundant datasets related to healthcare may represent identical situations or events. This is often observed in epidemiological notification systems, outdated systems and legacy systems, which may reference the same individual or event more than once. These datasets usually differ in their organization and have varying data dictionaries, increasing validation complexity and compromising data quality [Hinkel et al. 2022; Kim et al. 2019]. The heterogeneity of these datasets demands the use of methods for data linkage to optimize data interpretation and validation; in addition to this, incomplete or incorrect data represents another challenge for data linkage [Hinkel et al. 2022].

Different institutions and organizations may have their own health datasets, therefore data analysts must be aware of the differences between datasets. For example, changes in data formatting and standard units of measurement utilized to quantify data should be observed during data analysis [Rahm 2000]. Commonly, interpreting data proves challenging due to variations in numerical data format (where the decimal separator can be a period or comma), date representation (which can differ based on country of origin and time zone), and units of magnitude (such as weight, which can be measured in either kilograms or pounds). In this sense, the data dictionary is crucial for detecting these differences and avoiding risks and errors early on, even though it may not provide detailed descriptions.

These challenges are not the only obstacles when it comes to data extraction and interpretation, regardless of the area of study. Additionally, the healthcare sector presents its own specific set of challenges, which will be discussed below.

5.3 Other challenges of healthcare data and how to overcome them

Just as specialties in the healthcare industry diversify and expand with scientific advancements, health information systems also evolve as new technologies are developed, becoming more specific according to their application. As a result, it is now commonplace to find companies that specialize in developing systems for healthcare plans and eligibility, laboratory and imaging diagnostics, pharmacy services, multiparametric monitors, stock management, and procurement, among others. These systems may be used separately or in conjunction with one another. In practice, it is more typical for them to be interconnected to prevent the need for repeated work in certain areas. However, within this particular model, these systems function primarily as data silos, resulting in heightened ambiguity and unnecessary duplication of content [Pai et al. 2021].

To achieve effective integration of diverse information systems and manufacturers, besides the use of dictionaries, the use of communication protocols and health terminologies that facilitate this process at a higher level, known as interoperability, is essential [Pai et al. 2021]. The HL7 standard is widely recognized as one of the most commonly employed communication standards in interoperability solutions. Originally established in the late 1980s, the HL7 standard was developed with the objective of digitally connecting hospital areas and standardizing message exchange between sectors, inspired by computer network communication models. Currently, the standard has two versions: HL7 v2.x, based on standard and uncomplicated text message exchange, and HL7 v3, also known as Fast Healthcare Interoperability Resources (FHIR), which is utilized by various information systems worldwide [HL7 International 2023].

Initially, information system manufacturers were hesitant to adopt this open and widespread interoperability standard despite its numerous benefits. This was primarily due to the fact that a portion of their architecture would be exposed in a more open manner and could potentially undermine their monopoly within healthcare institutions. With the growth and global dissemination of the standard during the 1990s, hospitals started to require functionalities that were consistent with the standard [Simborg 2023]. The HL7 standard serves as a template, constituting one or more formats for the organization, reporting, and distribution of data. Nonetheless, this template is dependent on the content that populates it, and this is where terminologies come to play this role.

Terminologies play a critical role in unifying concepts around a standard idea. National initiatives exist to establish a shared medical vocabulary that facilitates the seamless exchange of health information between the state and health plans. In Brazil, the “Agência Nacional de Saúde Suplementar” (ANS) created the “Terminologia Unificada da Saúde Suplementar” (TUSS) for this purpose. Other commonly used international terminologies include:

- Systematized Nomenclature of Medicine - Clinical Terms (SNOMED-CT): This is the most complete terminology in the health field [Calado 2023], and the most comprehensive due to its broad representation of clinical terms [SNOMED 2023].
- Logical Observation Identifiers and Names (LOINC): LOINC is a widely used standard terminology for expressing clinical observations and laboratory terminologies [LOINC 2023].
- International Classification of Diseases (ICD): The ICD is a standardized terminology used to represent diseases and health-related issues. Currently in its eleventh revision, it is widely used; however, the tenth revision remains in use as well [WHO 2019].
- Global Trade Item Number (GTIN): This is an internationally recognized term used to uniquely identify traded materials [GS1 2023]. It is important to note that both terms serve as unique identifiers for traded materials. A similar but more regionally used term is the Mercosur Common Nomenclature (NCM).
- The Open Electronic Health Records (OpenEHR) standard began as an international project in 2003 and is currently maintained by an active community. This community provides freely available interoperability standards based on archetypes, artifacts, and subsets of terminologies (OpenEHR 2023), such as those listed above. In addition to providing interoperability standards, it also offers tools that require minimal coding, enabling rapid development and implementation of clinical models in institutions (OpenEHR 2023).

The purpose of this chapter is to demonstrate the intricate nature of health information systems, particularly with regards to the diverse range of information systems that must collaborate effectively to meet the hospital's targets. For this cooperation to be possible, these systems must utilize identical standards and terminology. Measures like these decrease the intricacy of interpreting data from health institutions, yet do not completely eliminate it. The following section will provide further context for another

factor that reinforces this lack of simplicity.

5.4 What additional challenges do long-term studies pose?

An answer to this question derives from *The Mythical Man-Month*, a book by Frederick P. Brooks, Jr. first published in 1975 [Brooks 1975]. As a computer engineer at IBM, Brooks stresses that information systems are not created, but built. This slight modification in wording provides an incremental outlook that typifies these systems, and thereby acknowledges that information systems constantly change and evolve. This state of continuous evolution applies to the entire information system. Due to the variety of manufacturers, it is common for hospitals to replace the entire information system in one or more areas. This may require total or partial migration of data from the previous system to the new one to avoid data gaps, which would compromise the chronological view of the data.

Part of the changes and developments in information systems are driven by legislation aimed at meeting public policy requirements. In Brazil, recent examples include:

- Changes in the systems for compulsory notification of Severe Acute Respiratory Syndromes, which was necessary because of the COVID-19 pandemic; this added new etiological agents and changes in disease criteria and diagnosis [Silva et al. 2022].
- The Social Name and Gender Identity of individuals were added to health data systems after publication of Decree 8727 of April 28, 2016 by the government [Brasil 2016].
- Mandatory identification of ethnic and racial identity in official worker documentation data [Brazil 2023].

The examples given above serve to contextualize the fact that changes in information systems were necessary to accommodate new data at different times. It is important to note that the absence of data collection before these laws and decrees does not indicate the non-existence of data. This understanding is crucial for interpreting data chronologically and avoiding bias. This challenge is particularly daunting in studies that integrate data from diverse sources [Harron et al. 2014].

5.5 Final considerations

Considering the rapid expansion of scientific knowledge, and medicine being at the forefront of this progress, the health sector will have access to increasingly specialized data for extraction and interpretation. Notably, advances in biosensors, genomic technologies, and molecular diagnosis are already impacting the amount of data available [Pathak et al. 2011]. Health institutions must be ready to store, analyze and use these data.

The increasing digitalization of hospital processes and automated data collection through sensors facilitate the digitalization of data in a cost-effective and highly accurate manner. This plays a crucial role in the subsequent extraction and interpretation of data [Tedesco and Konzen 2022].

It is crucial to recognize that the quantity of data collected does not necessarily equate to enhanced accuracy or reliability. It is also important to consider that the data gathered today will undergo countless future analyses, making long-term planning essential. Thus, it is imperative for organizations to engage in proactive discussions on data governance with both society and academia, establishing protocols and standards grounded in interoperability as a central tenet of any data initiative. Only then will we possess more uniform and non-repetitive data to advance public policies, steer hospital administrators, lessen operational expenditures, and deliver an improved service to the population.

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6 Mechanical evaluation with guarantee of printability of a Minimum Viable Product to produce artifacts in hospital scenarios: how Manufacturing 4.0 can bring successful results for healthcare management

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Abstract:

The coronavirus disease 2019 (COVID-19) pandemic led to severe shortages of essential medical equipment. Supply chains collapsed worldwide, which directly affected healthcare providers and patients in urgent need of medical attention. This study aimed to evaluate the impacts of Additive Manufacturing (AM) on autonomous fabrication within the hospital environment, integrating metallic elements (with biocidal properties) into resin submitted to photopolymerization during fabrication of medical devices. The methodology used to obtain a Minimum Viable Product was based on the synthesis of silver nanoparticles, followed by their incorporation into a light-curing composite resin matrix exposed to the Digital Light Processing (DLP) 3D printer. The present work also proposes combining AM with clinical engineering, prospecting: (i) the budgetary impact of Manufacturing 4.0 to replace items in a scenario of shortage or interruption in the supply chain; and (ii) the health management challenges putatively overcome by implementing makerspaces in hospitals.

Keywords: Manufacturing 4.0; 3D printing in hospitals; Healthcare management; Silver nanoparticles.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

6.1 Introduction

We faced the COVID-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Since its initial stages, the World Health Organization (WHO) has shown its concern with the possibility of mutations, keeping the Variants of Concern (VOCs) under surveillance and monitoring, as they are considered dangerous when preventive measures lose their efficacy. On the other hand, the decrease in the number of deaths and the decline in the totality of new cases resulted from prophylactic strategies with significant adherence from the population.

Production of medical devices resorting to Digital Fabrication does not emerge irrespective of the above situation nor from the unfounded attempt to tackle diseases in our daily lives.

The COVID-19 pandemic caused a severe shortage of essential Personal Protective Equipments (PPEs) and *medical devices*. Therefore, successful Digital Fabrication initiatives that contribute to healthcare management are not exclusively linked to the technical and interpersonal abilities of the team in charge, nor to the quality of machinery or supplies raised to develop the project.

Therefore, the present study idealizes Digital Fabrication in a hospital setting, to validate the process of producing a light-cured Minimum Viable Product that presents antibacterial and/or bacteriostatic characteristics, minimizing the presence of microorganisms and aiming the production of medical devices and functional equipment accessories. These accessories are currently not manufactured with this kind of 3D printing technology nor with the above characteristics.

Integration between Clinical Engineering and Digital Fabrication spaces located in hospitals and led by public universities enables: (I) manufacturing autonomy for engineers to produce customized and functional devices that could improve the healthcare frontline; (II) excellence in medical service for the patient who will receive treatment with a medical device (retaining functional properties) made especially to meet individual necessities and (III) cost reduction for hospital management, as some of the devices produced, may present antiviral, antibacterial or antifungal properties, reducing patients' hospitalization time. The ideas can be prototyped autonomously to rapidly meet medical assistance demands.

6.2 Methodology

The development of this study emerged from the idea of minimizing and/or avoiding cross-contamination of pathogenic agents for both the support team and care frontline. We perceived the need to create material presenting biocidal properties for 3D printing using the DLP process, and thereby measuring the impacts of Digital Fabrication for autonomous manufacturing in hospital settings. Thus, the mechanical, and antibacterial attributes of the material were evaluated. Results of the study include the elaboration of an open-source replicability protocol.

The activities were conducted at LIPECIN (Laboratório de Inovação, Prototipagem, Educação Criativa e Inclusiva) facilities at UFCSPA, together with the Santa Casa Hospital Complex in Porto Alegre, Brazil, and integrated both institutions in the search for tangible solutions in a hospital context. Additional steps were carried out at the Pharmacosciences Research Laboratory at UFCSPA (Raw Material Synthesis), Physical Metallurgy Laboratory (LAMEF) at the Federal University of Rio Grande do Sul (Mechanical Tests), and Microbiology Laboratory at Santa Casa, Porto Alegre (Microbiological Tests).

A flowchart was elaborated to show the way each stage was organized and developed to achieve the proposed purposes (Figure. 1.1).

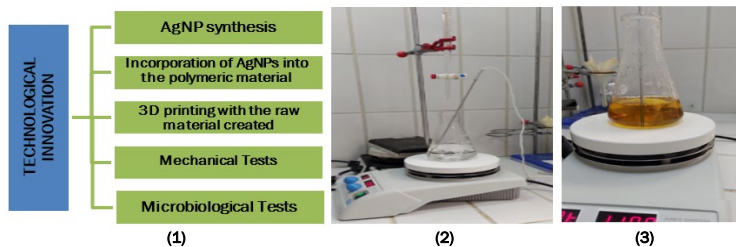
6.2.1 Synthesis of Silver Nanoparticles (AgNPs)

The method used is known as Turkevich method [1], which was proposed in 1951 to synthesize gold nanoparticles, but can be used for other metallic nanoparticles as well. It consists of using a reducing agent, in this case, sodium citrate, controlling the size of AgNP by supervising the temperature and agitating the reaction.

For the procedure for obtaining the AgNPs, silver nitrate 0.1N was used to synthesize the samples. It was necessary to adjust its concentration, so 1.25ml of silver nitrate was diluted in 125ml of osmosis water, so that we achieved the concentration of 0.1mMol.

After preparation, the solution of 125ml of AgNO₃ was put into a heater with magnetic agitation, configured at 100 °C and 1100rpm. After 25 minutes, the solution came to a boil. After that, using a volumetric pipette, 5 ml of 1% sodium nitrate was dripped into the solution at the speed of one drop per second. The mixture started changing coloration from the first minute until it reached an amber-yellow coloration six minutes after the deposition of sodium citrate had started. (Figure. 1.2).

Fig. 1. (1) Research design; (2) Deposition of Sodium Citrate; (3) Synthesis of AgNP.



Such coloration demonstrates the formation of silver nanoparticles. Because of that, the mixture was removed from the heater and put into another agitator to maintain the agitation until it reached room temperature (Figure. 1.3).

6.2.2 Incorporation of AgNPs to Polymeric Material

After the synthesis of silver nanoparticles, they were incorporated into the polymer to produce the raw printing material, which is done by activating the resin through a colloidal mixture of AgNP. This way we have the input for the next stage.

As for the mechanical tests, a proportion of 0.5% and 5% of the weight was used. Thereby we are able to obtain a Minimum Viable Product (MVP), which retains the mechanical properties so we can analyze it microbiologically.

For the resin, the base material for printing, we used a Beaker and Erlenmeyer, to separate 100ml of biocompatible resin in the Cosmos Splint model in each. The silver solution was added to the liquid resin in both glasswares, specifically, in proportions of 0.5 ml to 0.5% and 5 ml to 5%. Once again, the solution was heated and agitated to obtain a homogeneous blend (amalgam). The 5% solution reached homogeneity after 10 minutes of being agitated at 1500 rpm at 40°C. The 0.5% mixture, on the other hand, reached homogeneity by being agitated for 10 minutes at 1500 rpm at 60°C.

6.2.3 Specimens 3D Printing and Mechanical Tests

After silver nanoparticles had permeated the polymeric matrix of the resin, it was required to evaluate if any alteration could have happened affecting the mechanical properties of the resin so that a Minimum Viable

Product could be made. Therefore, the norm from the American Society for Testing and Materials, ASTM D790 (Standard Test Methods for Flexural Properties of Unreinforced and reinforced Plastics and Electrical Insulating Materials) [2] has been followed.

Tridimensional specimens were modeled on the Autodesk Inventor software, following the norms and, using the raw material prepared in the last stage, we started the 3D printing process using a DLP. For the specimens' dimensions, as it encompasses validation for any kind of printing and molding materials (thermoplastic and thermosetting), the dimensions for specimens specified in D790 for molding materials are 12,7mm width, 3,2mm thickness and 127mm length.

The printed parts were cured in a UV chamber within a washing and cure machine. The specimens were exposed for 15 minutes to a frequency spectrum of 405nm.

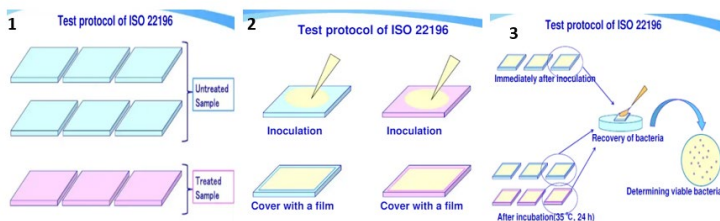
The flexural test was performed using a rectangular cross-section specimen resting symmetrically on two supports on a flat position, and a force was applied via a die which was found in the center position between the two supports. The rate of movement was 1.37mm/min. Nineteen specimens were printed, six in resin with the addition of 0,5% of silver nanoparticles incorporated to its matrix, six in resin with the addition of 5% of silver nanoparticles incorporated to its matrix and seven with pure resin.

The specimens were flexed until rupture using the parameters defined by the supports and the velocity of the trial, with the usage of a hydraulic servo machine and coupled with a load cell of 5kN.

6.2.4 Microbiological Tests

Microbiological tests were conducted following the guidelines of ISO 22196:2011 [3] with in-lab culture medium formation to prove the efficacy of the biocidal/antiviral action of the nanoparticles. Nine samples were printed, three of them with AgNP incorporated in resin structure and six samples of pure resin. That is because half of the non-treated samples were used to measure viable cells right after their inoculation (time zero), and the other half were used to measure viable cells after 24 hours of incubation. In bacterial tests, vines used from *Staphylococcus aureus* and *Escherichia coli*, were chosen following the norm (vines ATCC 6538P and ATCC 8739) (Figures 2.1-3.3).

Fig. 2.1, 2.2 and 2.3. ISO 22196 Protocol - Source: Japan Food Research Laboratories



6.3 Results and Discussion

6.3.1 Mechanical tests

It is noticeable that the resistance to flexing is lower when silver nanoparticles are added. For comparison purposes, technical information on the resin was collected. It was noticed that the flexural tension the specimen can bear is lower than the one presented in the leaflet, even when in pure resin. ISO 20795-1 [4] classifies the polymers and copolymers used for denture basis and specifies their requirements, which is not an object of this paper. On the other hand, ASTM D790 is more generalist, evaluating the flexural properties of any polymer. In other studies that were read, about orthoses and odontology supplies shaped with photopolymerization, present similar results to our study.

6.3.2 Microbiological tests evaluation

Regarding microbiological tests, the test in time zero without treatment had bacterial growth of both *Staphylococcus aureus* and *Escherichia coli*. It was noticed that there was growth in the colonies of bacteria in the culture medium, proving the quality of the inoculum. After 24 hours after seeding, the colony-forming units were counted.

For specimens printed in resins with and without silver nanoparticles, inoculated with the bacteria and incubated for 24 hours there was no bacterial growth in the seedings. By that, the experiment was repeated, but instead of just removing the film and making the first dilution, the whole specimen/inoculum/film and T.A.T. broth went through sonication, with an equipment called sonicator, so that, if bacteria were adhered to the specimen's surface, it would cause their detachment, enabling the

collection of the T.A.T. broth and the seeding in the culture medium.

The results were the same, as there was no bacterial growth resulting from the seedings. Therefore, because the resin was biocompatible, we sought to understand its composition and norm requirements, considering there was no bacterial growth in the specimen made out of pure resin.

Part 5 of ISO 10993 [6] rules the test for in vitro cytotoxicity. As by definition, cytotoxicity is the harmful property of a substance in relation to cells [7].

Rua (2013) [8], states that all monomers, which are molecules that form a basic unity of synthetic polymers, are cytotoxic. Due to the patent of the resins, we have little information about their composition. Evaluating the available information on the manufacturer's website, the resin used is composed of monomers and oligomers, indicating the possibility of it being the cause of the bactericidal effect seen on the tests.

Table 1. Printing costs by DLP process per hour

	Cost(R\$)	Capacity	Quantity of Work	Cost per unit	Cost per hour
Equipment	R\$ 8.000,00	-	20.000 hours	R\$ 0,4/h	R\$ 9,523/h
Electricity	R\$ 0,85/kW	0,145kW/h	-	R\$ 0,123/h	
Human Resources	-	-	-	R\$ 9,00/h	

Obradović-Djuričić *et al.*, (2011) [9] state that the photopolymerization of monomers in a matrix comprehends the opening of the monomer's double bounds and results in a process of cross-linking. As a consequence, all monomers should be converted into polymers during this process.

Nevertheless, during this process, the transformation of monomers into polymers is commonly not complete, which causes the lack of reaction in some double bounds. They are called residual monomers, which are released to the external environment [10] and [11].

Chia (2015) [12] affirms that one of the additional challenges in a photopolymerization process is that photoinitiators may be cytotoxic. Álamo (2020) [13] concluded that the resins for 3D printing from MakertechLabs and Yller present a cytotoxic effect over the oral mucosa cells in a similar

manner to what the same author observed in acrylic resins.

In order to obtain real proof, a specimen was printed in the same mold used in the same microbiological tests done before, but with a common resin for 3D printing, which is not biocompatible. The tests were made the same way as described before, but on a smaller scale, using only 3 dilutions to improve the understanding of the inoculum's behavior. The result, after 24 hours, was the same as the tests previously done, where there was no bacterial growth.

It is not possible to affirm whether any of the resin's composites caused bacterial death, as we had no access to the technical information related to the resin's composition.

6.3.3 Implications for Management

Considering the specific objective of evaluating the budgetary impact of the device's production and printing processes, in terms of cost reduction and permanence in hospital rooms, the present study enabled to map some implications for management and maintenance in a hospital unit.

As identified, there was no bacterial proliferation or formation of biofilm on the printed specimens' surface; as known, there are costs for disinfection and/or material acquisition. It is in the interest of the hospital complex, the possibility to alter or improve the disinfection process at Sterile Material Center as an alternative to cost reduction in detergent, electricity, vapor, equipment acquisition, operational teams, and others, accounted in the sterilization process (cost consultation on National Health Fund - Acquisition of Sterilizer - R\$ 309.316,00 + Acquisition of Thermodisinfectant - R\$ 350.900,00 + Physical infrastructure and personnel, results in an Average Cost of a Sterilization Cycle - R\$ 50,00). The values were extracted from National Health Fund website, SUS (Sistema Único de Saúde) regulatory agency for funding of medical equipment (Brasil, 2023) [14] and from Tasy health management system, used at Santa Casa, Porto Alegre.

National Health Surveillance Agency (ANVISA) in Brazil, through RDC nº 15, 2012 [15] provides good practices requirements for processing healthcare products classified as semi-critical (those that have contact with non-intact mucosa and skin or intact mucosa, as, for instance, products for ventilatory support), regulates in its article 12, the high-level disinfection after cleaning before it is made available for another patient's use. This disinfection is a physical or chemical process that destroys most of the

microorganisms.

Components made of this material wouldn't need this kind of cleaning process. It would be a change in welfare protocols in hospitals, directly implying cost reduction in all process chains that involve the sterilization sector, as well as the purchasing sector, as the costs and time involved in prototype production become clear (Table 2).

So, when we evaluate printing ventilatory parts (connectors, diverters), printing time is in the order of hours (information is available in the prototyping software). In order to acquire via the usual process of purchasing, we depend on the budget sent by a supplier, internal approval and shipment, a process which surpasses a month between its fabrication and receiving the item.

Table 2. DLP printing costs ventilation circuit connector

Printing Hours	Hour cost	R\$/ml *	Resin (ml)	Total
10	R\$ 9.523	1.6	36	R\$ 152,83

*Cost of resin used BRL 800.00 (manufacturer's website), 500ml.

We can estimate the printing cost per hour, by accounting the acquisition and operation costs. Understanding that the DLP process would take some hours, we can evaluate the printing cost of a prototype with a hospital bed just waiting for an equipment part acquisition.

During the pandemic, we resorted to Additive Manufacturing for the replacement of a spare part, which was a ventilatory circuit connector, which was difficult to supply, with the shipment exceeding one month. The commercial value was R\$ 250,00 (data from purchase system of Santa Casa de Porto Alegre). Modeling it in DLP, we have the printing value (see Table 3).

At that moment of the pandemic, the part was printed in Nylon (FDM) with the cost as seen in Table 4. On the other hand, the cost of a daily rate in ICU from SUS passed on to the hospital is R\$ 700,00 (Brazil, 2023) [14], while the daily rate for a private ICU in Brazil during pandemics was R\$ 2.234,00 [16].

Table 3. FDM printing costs ventilation circuit connector

Printing Hours	Hour cost	R\$/m*	Filament (m)	Total
5,76	R\$ 9.523	3.84	5.57	R\$ 76.32

* Consultation carried out on the website: <https://usefixit.com.br/categoria-produto/orteses-3d/>

Comparing the two models, it is clear that the privilege of making specific spare parts that need replacement for equipment maintenance can avoid revenue losses and, most importantly, the patients can rapidly receive medical care. This way, there is a new perspective for supplying, less production cost, reduced time spent for manufacturing and the easy access by any user, which might be able to partially solve a recurring problem in SUS, in which corrective maintenance of medical equipment is dependent on the availability of spare parts on the market, affecting hospital management [17].

We also have the freedom to produce other types of inputs that could directly affect the patient's hospitalization time. During this period, in an ICU, when the patient is intubated, bacterial colonies form on the patient's trachea, causing what is called ventilator-associated pneumonia (VAP) [18], increasing hospitalization time [19].

One paper [20] reports positive experiences with the low-cost modeling of video laryngoscopes with a unitary printing cost of around R\$ 65,00, while the cost in the market for SUS is stated to be R\$22,525.00 (<https://consultafns.saude.gov.br/#/equipamento>). The cost for the same development, validation and production of a video laryngoscope at LIPECIN, at UFCSPA, did not surpass R\$ 100,00.

Besides the item cited above, another huge concern in the period after the pandemic is the lack of availability of orthotics, prosthetics and special materials (OPSM) in hospital supply chains, of which the necessity increased by 25.6% according to the Brazilian Association of Innovative Health Industry [21]. This way, an opportunity emerges, to develop these inputs with reduced costs [22]. Thus, in addition to meeting the demands for accessories and parts, this work suggests another line of assistance to the patient that can be developed through the hospital FabLabs.

Within the scope of the Unified Health System (SUS), the local 3D printing of OPSM parts could help the reduction of time in providing medical care. From the financial point of view, it could contribute to a reduction in the hospital budgetary imbalance caused by the lag on SUS' cost tables. The budgetary transfer from SUS for an "*aeroplane type axillary-palmar immobilization static orthotic*" is R\$290,00 [14] and does not remunerate professional services, comparing it to a 3D printed model, the latter costs R\$ 100,00.

Even after a global supply chain collapse, striking several items after the pandemic and directly affecting hospitals and patient morbidity, the

customization of parts that are to be delivered to the final user eliminates delays, bureaucracy, time-loss that are involved in the supply chain process [23]. That encourages the development of maneuvers that eliminate the acquisition process of inputs and medical equipment parts and the 3D printing of parts inside medical facilities.

However, regulatory issues related to reverse engineering, which is a process of recreating an existing process, were not evaluated in this study. Moreover, a medical device is composed of parts and they are either regulated independently or considered a medical product to be under ANVISA's regulation.

6.4 Conclusions

We aimed to contribute to the welfare process, associating Additive Manufacturing to Clinical Engineering, to reduce the waiting time for replacement parts of medical equipment, as well as to reduce acquisition costs of inputs and accessories using 3D printing as artifact provider, which is a difficulty of the public health system (Sistema Único de Saúde).

Scientific knowledge about cross contamination, construction of accessories with biocidal agents, or even the suppression of a costly process for the hospital, associated with the innovation potential directly linked to the internal processes of each institution, are the main contributions expected of this study.

On that account, we aim to optimize the adhesion of silver nanoparticles onto the polymeric surface, to produce a ventilatory circuit in real size that could have an antiviral, antifungal and antibacterial spectrum of action.

The development of a local structure, inside the hospital setting, dedicated to Manufacturing 4.0, emerges as an important alternative to accelerate the repositioning process of an accessory or item necessary for an equipment's functioning, lowering the impact on welfare and meeting the needs found in SUS medical care settings, where the difficulties caused by internal processes impair the working process of health professionals, affecting the medical care for patients. Another strategic aspect related to the incorporation of development of medical devices build through Manufacturing 4.0 is about the intellectual properties that are generated, which starts to modify the supply chain of some accessories, performing on the severe shortage of inputs encountered by SUS, as mentioned before. The positive impact will occur as there is free access to a database of 3D

printing files, for knowledge exchange between different hospitals.

Finally, this study has presented a new viewpoint to emphasize the strategic role of Clinical Engineering, showing how Manufacturing 4.0 can be inserted in the hospital context with the intent of enhancing medical care, as well as undertaking professionals who are related to healthcare. The study may also contribute to the improvement of welfare processes inside a healthcare establishment, affecting time and costs of production and the usage of raw materials, to adopt practices that help in service availability.

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7 Information and Communication Technologies, Accessibility, and Inclusion: a Health Technology Model for Users Facing Limitations

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Abstract:

There are still many barriers to the use of information and communication technologies (ICTs) by users facing limitations because they do not always have their needs met in the design of ICTs. So, this study aims to propose a model for the design of health ICTs for users facing limitations. A systematic review of the literature and a workshop were performed, and categories were found and discussed as important structures in the design of technologies for users facing limitations. A model was built based on the categories, considering inclusive design. Although it brings a broad scope of inclusion of all people, it allows a specific look at different limitations. It brings advances in the sense that the design of ICTs for users facing limitations must consider not only technical aspects but must be supported by support structures.

Keywords: accessibility; inclusive design; Information and Communication Technologies; users facing limitations; model.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 10. Reduced Inequalities.

7.1 Introduction

Disability is experienced by 15% of the global population, resulting in around 1 billion people with disabilities (PwD) worldwide. This condition is exacerbated by population aging and the increase in chronic diseases [WHO, 2021]. Therefore, disability is part of the human condition, since almost everyone may experience some life-long limiting condition [Uromi and Mazagwa, 2014]. Due to the existing limitations, caused by the barriers that PwD find in many of the spaces in which they interact, these people struggle to access services and healthcare [Maia, 2013].

Information and communication technologies (ICTs) have been identified as facilitators in healthcare for people facing different limitations [Krysta et al., 2021]. However, there are still many barriers to the use of these ICTs by PwD because they do not always have their needs understood and met in the design of ICTs [Moon et al., 2019]. These barriers may become even more present in a context in which multiple vulnerabilities are present, such as the case of elderly people who face limitations arising from aging [Rosenberg et al., 2009] and patients with chronic diseases that cause disabilities or with previous disabilities that are potentiated by the disease [Samal et al., 2021].

While these technologies are helpful with issues related to access to health for users facing limitations, they need to be accessible, given the diversity of functions and structures of the human body, its abilities and its context, according to each individual [Henni et al., 2022]. If there are no parameters of accessibility in the design of ICTs, the digital divide appears, which consists of the division between people who can use digital resources and people who cannot [Dijk, 2020]. In this study, accessibility will be understood according to its etymological meaning, which is the quality of being able to be reached or inserted, being easy to obtain and use, and being easily understood or appreciated [Oxford English Dictionary, 2023]. This is in line with the Web Accessibility Initiative (WAI), which contains strategies, standards, and resources to make the Web accessible to PwD [WAI, 2023].

This context is related to inclusive design, which seeks solutions that encompass as many people as possible, with special interest in vulnerabilities, disabilities, and limitations [Goodman-Deane, 2014]. In view of this, it is essential that the design of ICTs consider the use by the greatest number of people. To the best of our knowledge, there are no technology design models in the literature that consider structures for disabilities in

general. So, this study aims to propose a model for the design of health ICTs for users facing limitations.

7.2 Method

This study has a qualitative approach, with an exploratory character, consisting of a literature review and a case study. For data collection, a systematic review of the literature was first carried out and, in the second moment, a workshop was performed. The two moments were complementary for the structuring of a model of health ICTs to meet the specificities of users facing limitations.

7.2.1 Literature Review

The systematic literature review (SLR) followed the steps recommended by Arksey and O'Malley (2005). First, the main research question was defined: How are health ICTs structured to serve users facing limitations? In a second moment, the keywords and databases were defined, after initial tests. The keywords defined were: health* AND (disab* OR impair* OR "mobility reduced") AND ("ICT in health" OR "information and communication technolog*" OR "digital health"); considering the search only in abstracts, in Scopus, Wiley, Pubmed, Bireme, Embase, ScienceDirect and Web of Science databases. At ScienceDirect the search had to be carried out with minor modifications, because of the specificity of each database.

For the selection of studies, we followed the steps recommended by Moher (2009), based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines: identification, screening, eligibility, and inclusion. All steps were peer-reviewed to ensure study quality. The inclusion criteria defined by the authors were (i) articles published from 2017 to 2021, (ii) in English and Portuguese, (iii) published in journals, and (iv) in full. The exclusion ones were: (i) literature reviews, opinion articles, theoretical essays, meta-analyses, perspectives, commentaries, protocols, editorials/lessons from the field, correspondence articles, congress reports, view/personal points, position papers, and debates; (ii) duplicate articles; (iii) articles not dealing with technologies in a context of accessibility and limitation; (iv) articles not dealing with the health context; and (v) articles not dealing with the context of technologies.

After entering the inclusion criteria in the filters of the databases or manually, 2,052 articles were found in the identification phase. In the

screening stage, 1,220 records were excluded, resulting in 832 articles. After that, 147 duplicates were excluded, resulting in 685 articles. Abstracts of the 685 articles were first read, and 611 which were not in accordance with the theme of analysis were excluded. After that, the 74 resulting articles were read in full, and 41 articles were included in the systematic review, as they were in accordance with the theme and brought structures of ICTs to serve users facing limitations. To organize the data, we set up a table with the most important information about the articles. For data analysis thematic analysis was performed [Braun and Clarke, 2014] where categories emerged through both inductive and deductive approaches. The categories defined a priori came from the accessibility fundamentals recommended by the Web Accessibility Initiative [WAI, 2019].

7.2.2 Case Study

A case study was carried out in a private outpatient oncological service of a Brazilian hospital that assists 86 cancer patients. Observations and interviews were carried out in the service with patients, caregivers, and professionals, to understand patients' experience with the service, as well as critical points related to accessibility and inclusion, and opportunities for implementing technologies. A workshop was held as a design tool that generates ideas, concepts, and solutions to identified and presented problems [Lima et al., 2016]. The co-creation took place based on the themes of barriers to inclusion and accessibility to an oncology service, patients' experience during their health journey, technology solutions, and structures of ICTs to meet users facing limitations. This last theme was of particular interest for this study. The participants learned, performed creative and innovative problem-solving related to the specific issue [Ørngreen & Levinsen, 2017].

The workshop took place in March 2023, in a single 3-hour meeting at a university building, was conducted by two researchers, and brought together 10 cancer patients (in treatment or survivors), two caregivers, five professionals from oncology services, seven people with disabilities (two blind, three deaf, and one person with a physical disability), and two specialists in the field of design and disabilities (one of them was also a sign language interpreter).

The workshop followed the design thinking method based on the four steps suggested by Kelley and Kelley (2013): 1. Inspiration; 2. Synthesis; 3. Ideation and experimentation; and 4. Implementation. Data were collected

through photographs, observations, field notes and recordings, with the consent of the participants and prior signature of an informed consent form. First, the two researchers raised awareness about the subject, then the participants were separated into four groups (one of the groups was formed only by the PwD and specialists), and at the end a debate was held between all the groups, raising points of interest. Data were analyzed using thematic analysis [Braun and Clarke, 2014]. Concerning research ethics, the study was approved by the Institutional Ethics Committee.

7.3 Results

The themes were categorized a priori based on the WAI material and a posteriori with empirical categories based on the data of the SLR and the workshop. The WAI thematic categories found in the collected data are: perceivable information and user interface; operable user interface and navigation; understandable information and user interface; and robust content and reliable interpretation. The themes that emerged from empirical data are: custom technologies; training; use of design approaches; inclusion of others in the technology implementation process; playful design; privacy guarantee; and accessibility beyond technology.

7.3.1 Operable user interface and navigation

In terms of user-friendliness, the focus is on devices that are easy to use and require fewer steps, offering various ways of input beyond keyboards. This includes voice-guided tools and motion-based interfaces, accommodating users facing diverse limitations [Biehl et al., 2021]. During a workshop, a participant with visual impairment emphasized the value of sensors in ICTs to enhance device accessibility. Additionally, they proposed an intuitive button in health technologies, functioning as a support channel for users unfamiliar with tech, offering information or assistance as needed. Studies also underscored the significance of bigger screens [Najm et al., 2020] and allowing sufficient time for each user to navigate devices [Tiersen et al., 2021], particularly for those facing limitations, as crucial elements for ICTs.

7.3.2 Perceivable information and user interface

This theme concerns adapting the format of information for better use by more people. This means that there are crucial many possibilities of use for users facing limitations to be able to use health ICTs. The possibility of

increasing font size and style [Kairy et al., 2021], the availability of options for multiple senses (visual, audio, and touch) [Gagnon Shaightz et al., 2021], and the presence of language of signs in videos and screen readers [Dai and Hu, 2021] were some of the examples of easy adaptation of technologies. At the workshop, the PwD group discussed that ICTs such as mobile health applications should always have audio options, to better guide a blind user. Blind participants commented that in their daily lives they usually use headphones and the accessibility feature on their cell phones, being able to communicate with anyone and get anywhere. This way, blind people can be better guided in any environment using technology.

7.3.3 Understandable information and user interface

This theme is related to the ease of understanding of the information available in the technology, considering accessible language, clear and concise texts, and avoiding errors by the user. Avoid a lot of text [Kairy et al., 2021], medical jargon and technical terms, return function [Gibson et al., 2019], and provide feedback to users after performing a task to situate them on its correct use [Tiersen et al., 2021], are some of the solutions that increase the user's understanding of information available in ICTs. Workshop participants also emphasized that scientific language hinders lay people's understanding. In addition, the study by Martin-Hammond et al. (2019) states that for elderly people facing limitations, simple and direct language, considering a lay audience, is essential for their engagement with technology. Furthermore, the ICT should not ask many questions, with shorter content, to capture attention and be easy to understand.

7.3.4 Robust content and reliable interpretation

Compatibility of the content with different tools and browsers was observed only in the study by Babatunde et al. (2020). In the workshop, this theme was also perceived when cancer patients were encouraged to reflect on technologies in health services. They reported the difficulty of implementing technologies because there is no data integration and system interconnection. Thus, a process that is already difficult for users facing limitations, becomes even more difficult, since these patients do not have all their health data available in a single application. This was particularly important for an elderly patient undergoing cancer treatment, who pointed out that it was difficult to let go of medical records on paper, because when she goes to different doctors, they do not have access to an integrated

program with all the patient's data.

7.3.5 Custom technologies

The possibility of adapting technology to specific needs is the central point of custom technologies. In the workshop this was brought up by the disability group and experts as crucial for the use of ICTs by different people. The articles pointed out this theme, emphasizing the importance of knowing the needs, allowing representation in the technology, with options for their own avatar according to how the person sees themselves and the option to perform technology activities sitting or standing, for example [Gagnon Shaiget et al., 2021], and an option of having a disability mode in technology, helping blind users and other groups in use [Nimmolrat et al., 2021].

7.3.6 Training

User training for the use of technology emerged as crucial in reducing digital divide [Contreras-Somoza et al., 2020] and enhancing technology literacy [Christiansen et al., 2020]. Users emphasized the necessity of training to effectively utilize ICTs; without it, the consideration of other structural aspects in health technology design would be futile. Training took various forms: educational preparation before ICT use aligned with educational initiatives [Contreras-Somoza et al., 2020], periodic training [Rikard et al., 2018], device-specific training [Barlott et al., 2019], home visits by IT assistants [Jakobsson et al., 2020], educational intervention programs [Biehl et al., 2021], individualized face-to-face training with ongoing reminders [Rai et al., 2021], technical support during the use [Biehl et al., 2021], and tutorials [Gagnon Shaiget et al., 2021].

7.3.7 Use of design approaches

This theme emerged only in the analyzed studies in the SLR, bringing the focus that the in-depth understanding of the target population and its needs, and its involvement, as well as that of other interested parties, is fundamental for the design of technologies for users facing limitations [Giunti, 2018]. User-centered design [Park et al., 2019], co-creation with the user [Ferguson et al., 2021], usability testing and user feedback [Petrescu-Prahova et al., 2020] proved to be important for a better design of ICTs for these users. In addition, the study by Najm et al. (2020) highlights that, for health ICTs to be structured for users facing limitations, it is

necessary to involve patients in the development process.

7.3.8 Inclusion of others in the technology implementation process

This theme was found only in the articles and is related to the need to have other people with the users facing limitations for the implementation of the technology, since these people do not manage it in the place of the users, in order not to take away their independence [Barlott et al., 2019]. The acceptance by formal caregivers of the implementation of technologies [Contreras-Somoza et al., 2020], supervision and medical support [Urban, 2017], and triggering device warnings to caregivers [Anisha et al., 2020] are some of the structures considered important in this theme.

7.3.9 Playful design

Users facing limitations are more interested in using ICTs when ludic elements are associated, so that their use is facilitated. Inputting memory games in ICTs for patients with cognitive impairments, for example, proved to be an important resource for the user to be able to use ICTs, in addition to being a resource that assists in memory rehabilitation [Minen et al., 2021]. Funny images and memes [Barlott et al., 2021], Youtube, music [Chiu and Wu, 2019], intelligent voice assistants for on-device health issues [Martin-Hammond et al., 2019], and reward to motivate use [Gagnon Shaiget et al., 2021] were some of the structures suggested in relation to playful design. This theme is especially related to users with cognitive impairments. The study by Minen et al. (2021) points out that ICTs should be used to help people with neuropsychiatric conditions to engage in meaningful and pleasurable activities, such as cognitive stimulation and physical activities, as well as technologies to enhance social participation.

7.3.10 Privacy guarantee

This theme was evidenced only in the SLR, whereas many users facing limitations do not use ICTs due to distrust of the security of their data. Data protection and security [Biehl et al., 2021] and privacy security [Martin-Hammond et al., 2019] were considered points of attention for the design of health ICTs for users facing limitations. In the article by Urban (2017) the elderly were afraid that sensors could expose their daily activities, their sexual practices, and their lifestyles, and this could be embarrassing. The study by Kairy et al. (2021) found that despite the interest of individuals with physical disabilities to be interested in socializing with people going

through the same situation, they would like to know what information was being shared.

7.3.11 Accessibility beyond technology

This theme was addressed only in the workshop. The deaf group reported that, regardless of technology, the notion of accessibility needs to go much further. Before proposing technologies, it is necessary for designers and health professionals to understand how to include these users in health services. The group with disabilities was favorable to the implementation of technologies, but they showed concern with much deeper factors, prior to implementation.

Figure 1.1 shows the model resulting from this study, with the health ICT structure for users facing limitations. Thematic categories are arranged in the circles, which represent the structures that must be considered in the design of ICTs for users facing limitations.

7.4 Discussion

The proposed model considers users facing limitations in a broad way, without considering a specific disability but seeking to bring structures aimed at different users. The model is in line with inclusive design, in the logic of including as many people as possible in proposed solutions [Goodman-Deane, 2014]. In this perspective, the design of technologies must be thought of to encompass and enable the use of any person, regardless of disability. Otherwise, the use will cause limitations to the user, becoming a barrier, and not helping to include these people with greater health vulnerability.

The combination of different structures, such as the screen reader for blind people [Choi et al., 2020], sign language and captions for deaf people [Dai and Hu, 2021], augmented icons for people with visual loss, including the elderly [Park et al., 2019], the reduction of text and information, and the use of images and care with color contrast for people with cognitive problems to be able to understand better [Gibson et al., 2019; Babatunde et al., 2020] can direct the best design of technologies, encompassing different needs.

However, even if inclusive design seeks to consider all people in the proposed solutions, it is not always possible to design a single solution that meets all existing needs [Clarkson et al., 2007]. The model brings structures that, combined, can include as many people as possible, but thinking about

different solutions in ICTs to serve different users can also be a pertinent strategy for including many people. Different structures can be considered in more than one technology, to cover more users and more limitations, and the model allows us both a generic and a specific look at the different requirements of users with different disabilities.

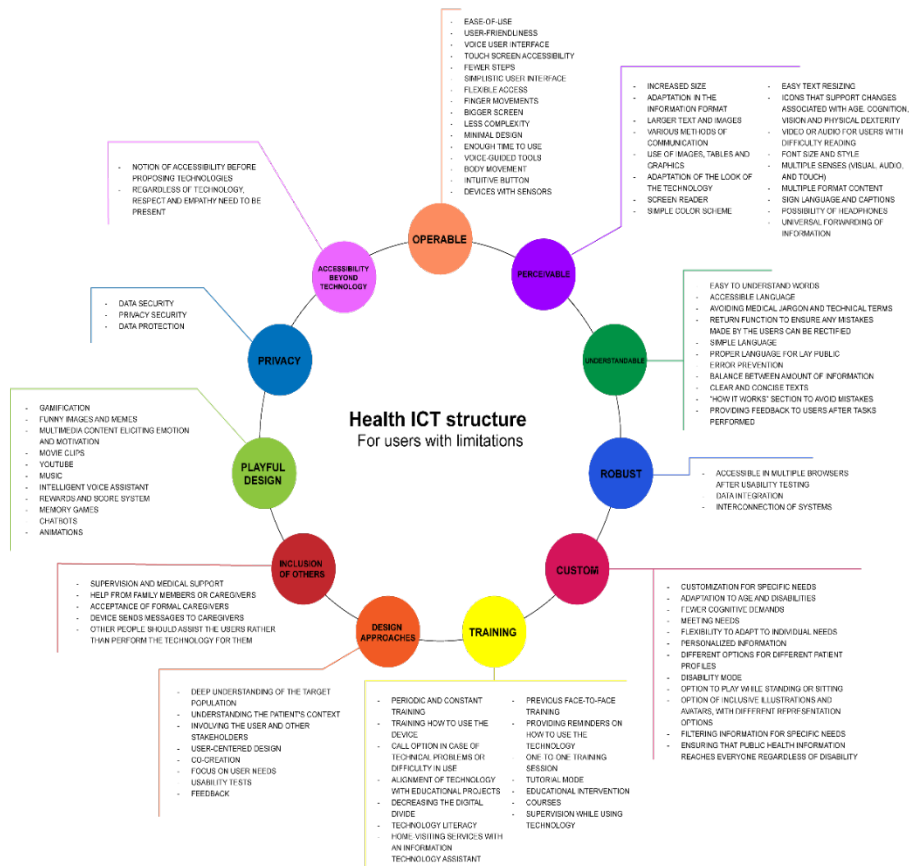
7.5 Conclusion

This study aimed to propose a model for the design of health ICTs for users facing limitations. The model was built based on each of the categories, considering inclusive design. Although it brings a broad scope of inclusion of all people, it allows a specific look at different limitations. It brings advances in the sense that the design of ICTs for users facing limitations must consider not only technical aspects, but must be supported by support structures, such as education for use.

The main limitation of this study is that we were unable to include more people with different disabilities in the workshop, due to impossibility/non-interest in participating. Future studies could complement the model, including the perception of even more users facing limitations in construction, since inclusive design seeks to include the requirement of as many people as possible in proposing solutions.

7 Information and Communication Technologies, Accessibility, and Inclusion: a Health Technology Model for Users Facing Limitations

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8 Standardized Communication in the Interdisciplinary Round with the Support of an Instant Messaging Application: Reducing Risks and Hospital Stay

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Abstract:

The use of structured interdisciplinary rounds in the hospital context is a care model that leads members of the interdisciplinary team to meet regularly, thus promoting interdisciplinary accountability. With technology evolving rapidly and playing a prominent role in the healthcare system, it is important to understand how instant message applications are used in hospitals and its potential effects on group practices and patient care delivery. The objectives are to assess the use of WhatsApp as a compliment of clinical round, through the length of stay (LOS), Injury Severity Score (ISS) and interdisciplinary team satisfaction. The results demonstrate the benefits to team integration, but some resistance to technology adoption. There is no evidence on the impact at LOS and ISS.

Keywords: Effective Communication; Interdisciplinary Round; Instant Messaging Application; WhatsApp; length of hospital stay.

Sustainable Development Goals (SDG): Goal 3. Ensure healthy lives and promoting well-being for all at all ages; Goal 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all; Goal 16. Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels.

8.1 Introduction

Ward rounds are essential for the management of hospitalized patients around the world (WALTON, 2019). They are made up of professionals from different areas who list problems related to patients and establish goals to be achieved by the interdisciplinary team, with a detailed and individual view of each patient with the aim of discussing, considering and making decisions about details and general management of care. (WU-FIENBERG, 2018). Topics commonly covered during the rounds include diagnosis, prognosis and treatment planning (GIRI, 2013). The adverse consequences of hospitalization, such as medication errors, hospital-acquired infections, preventable injuries, prolonged hospitalizations and preventable deaths, have encouraged the implementation of new models of interdisciplinary care that aim to address these issues by improving cooperation and communication between healthcare professionals. However, interdisciplinary care may be sporadic, unstructured and geographically fragmented, or there may be a lack of involvement from any team member or a lack of a communication protocol (BASIC, 2018).

Greater communication of clinical ideas, opportunities for team discussion, and a sense of partnership and support require not only increased information but improved delivery (WHITLOW, 2014). Although mobile technology (i.e., handheld devices that facilitate two-way communication or data transfer) has the potential to significantly improve teamwork and communication in hospitals, there are still important organizational, technological, and security challenges that must be addressed (BROMAN, 2017) like the technology adoption, application integration and sensitive patient data. WhatsApp is a device with enormous potential, as it allows greater interaction between people and has several features that facilitate communication and sending information between users (SANTOS, 2018).

The use of structured communication, such as a script or checklist, on face-to-face communication, together with the continuous assistance of WhatsApp, can improve interdisciplinary work and communication, reduce risks and length of stay and contribute to hospital management.

8.2 Hospitalized patients and length of hospital stay

Prolonged hospitalizations have been associated with both clinical and socioeconomic factors, as well as markers of increased disease severity, such as palliative care, length in the Intensive Care Unit, and need

for surgery. The multiple factors contributing to prolonged hospital stays pose a challenge for hospitals trying to control length of stay (HECK, 2020).

Currently, there is a growing concern among health institutions, whether private or public, for better results in health care, reflecting a competitive system, in which it is considered that the increase in the volume of care, the reduction of hospital stay, the reduction of care costs and good results are guarantees of survival in the health market (BORBA, 2006). The length of hospital stay (LOS) is one of the institutional quality indicators used to define the bed yield and productivity of each specialty.

Reducing excessive length of stay is an important objective for hospitals seeking to increase bed availability, maximize cost efficiency, and reduce complications, as the length of stay in the institution has consequences for the health and well-being of the person, increasing the risk of associated morbidity and mortality, given the increased risk of malnutrition, depression, falls, confusional states, iatrogenic infections and complications, decreased mobility, possible deep vein thrombosis and increased level of dependence. In addition to excessive bed occupancy, some other barriers are identified, such as operational delays that consist of delays in scheduling exams and waiting for follow-up and evaluations by specialized medical teams (ZHAO, 2018; RAMBANI, 2008).

Effective coordination of patient care by an interdisciplinary team is a key goal of patient-centered medical care coordination is particularly important for complex patients, or those with multiple comorbidities and social support needs. However, care coordination is often hampered by disjointed communication and the lack of a support protocol infrastructure. Interdisciplinary care planning has been proposed as a solution to improve team care for complex patients (ROTENSTEIN, 2016).

8.3 Severity score

In the last twenty years, several indices have been developed and refined to determine the severity of trauma, based on anatomical, physiological, and mixed criteria (MODAS, 2019; RAMBANI, 2008; GENNARI, 1995). By means of a uniform language, the severity indices allow, among other aspects, the comparison of morbidity and mortality between groups of patients whose trauma severity is similar. In this way, they favor the evaluation and comparison of the care provided by various trauma care services, the monitoring of the evolution of care over time, as well as the effectiveness of the measures instituted. The indices can assist

in the process of triaging patients, in the planning of services, in the distribution of human and material resources, and in institutional auditing. Among the indices developed to determine the severity of trauma in hospitalized patients, the Injury Severity Score" (ISS), has been recognized as the most promising, as it is endowed with sensitive prognostic power with a view to survival and mortality. The ISS was developed in 1974 by Baker and colleagues, and the severity score of the trauma is obtained using six regions of the body: head or neck; face; thorax; abdomen or pelvic contents; upper limbs, lower limbs or pelvic girdle and external surface. The ISS score ranges from 1 to 75. Higher scores indicate greater severity of trauma and, consequently, suggest longer hospital stay and demand from the interdisciplinary team, in addition to characterizing a higher probability of death (GENNARI, 1995).

By knowing and relating the causes associated with the prolongation of hospital stay, preventive care is promoted, seeking improvements in care and minimizing problematic situations (MODAS, 2019).

8.4 Healthcare management and technology

When you work with an interdisciplinary team with a qualified and solid knowledge base, you further narrow the margin for error and promote an organizational culture. The use of structured interdisciplinary circles is a model of care that leads members of the interdisciplinary team to meet periodically, thus promoting interprofessional accountability (BASIC, 2018).

These links created by the professionals of the interdisciplinary teams contribute to the organization, hospital management, quality, and patient safety. This work is essential to ensure the implementation, continuity, and maintenance of interdisciplinary communication and patient safety initiatives, as well as in the monitoring and dissemination of results associated with continuous improvement initiatives (OLIVEIRA, 2017).

8.5 Interdisciplinary communication and effective communication

Structured communication and the work of the multidisciplinary health team are understood as determinants of quality and patient safety. Thus, patient safety is one of the great challenges of health care nowadays and, therefore, the objective of health institutions is to reduce damage and risks, ensure the patient's well-being, which, when achieved, can also reduce the length of hospitalization and treatment. In this sense, among the set of measures to ensure safe care are the following of protocols and clear

and objective communication among health professionals, in order to minimize errors in care (OLINO, 2019).

Despite the advances, one of the biggest challenges has been the lack of communication during the care course of patients in health institutions, generating unwanted injuries, prolonged hospitalization time, adverse events and even death, which requires solutions with procedural changes and new technologies. Thus, effective communication becomes one of the international goals of patient safety and refers to the shared information regarding the care provided to the patient, involving the most diverse professionals in the hospital environment. Effective communication between healthcare team members happens when there is eye contact, active listening, confirmation of understanding of the message, clear leadership, involvement of all team members, healthy discussions of pertinent information, and the ability to accurately anticipate future problems. Investments and advances in information technologies have gained prominence in the search for effective communication, however, they do not replace verbal communication due to the richness of interactions. Thus, verbal communication continues to be essential for sharing information about patients, conveying urgency and highlighting situational nuances. In this sense, structured interdisciplinary rounds are resources that favor communication between team members, as they can reduce the length of the patient's stay in the hospital and improve quality indicators (GUZINSKIA, 2019).

Studies have directly shown that care management has been the main focus of patient care and the rounds of the wards that involve groups of professionals from different areas of health, discussing, deliberating and making decisions is an important part of this process (GIRI, 2013; MOYSE, 2013).

8.6 Final Remarks

Health care is a composition of the system of service providers and actions taken within this system aimed at improving health and well-being. Good quality means serving patients with technically appropriate services, with good communication, shared decision-making, and respect for individual culture (Campbell, 2000).

The interdisciplinary team will benefit from another communication resource, with easy and quick access for daily demands. Discussions,

clarification of doubts, announcements and everything that is pertinent will follow at various times of the day and not just once a week.

The patients involved will benefit from the resolution of their definitive treatment being carried out in a supervised and faster way, adding to this, quality of life and minimizing risks and symptoms of depression due to the frequently observed length of stay. In addition, they will feel welcomed in the hospital environment and with the certainty that they are receiving effective care and consequently adding value to a positive evaluation to the institution.

8.7 Contributions for the 2030 Agenda for Sustainable Development

In general, the discussion presented at this chapter contributes to Goals 3, 8 and 16 of the 2030 Agenda for Sustainable Development (SD). The Goal 3, “ensure healthy lives and promote well-being for all at all ages”, specify to halve the number of deaths and injuries from road traffic accidents. In this chapter, patients with trauma, especially by traffic accidents are the main focus.

Sustainable Development Goal 8 aims to “promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all”, describing the social dialogue, among others, an element of the new 2030 Agenda. This chapter advocates the importance of the participation of the entire interdisciplinary team in a productive, democratic and healthy group, where each one has the work that deserves.

Finally, the Goal 16 - Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels, and the SDG target 16.7 aims to “Ensure responsive, inclusive, participatory and representative decision-making at all levels”. By using a widely used instantaneous message platform, as WhatsApp, and opening the participation to all involved professionals, the organization creates means to qualify the decision-making.

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9 Patient Navigation and Health Technology as allies in Comprehensive Care

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Abstract:

Coping with cancer permeates several barriers, whether administrative, financial, therapeutic or even self-management. Patient navigation comes as a care methodology that proposes assistance and monitoring aimed at reducing obstacles to accessing services, as well as managing self-care for a better clinical outcome. This work model is linked to telenursing, where the professional “navigator” combined with the multidisciplinary team plans and executes the steps of coordinating comprehensive and individualized care, using information technologies, improving the care process.

Keywords: Biomedical Technology, Cancer, Patient Navigation, Telemonitoring, Telenursing.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

9.1 Introduction

Cancer navigation emerged in the 1970s in the United States as a result of a study that identified the need for active and structured monitoring of women with cancer due to the existence of previous vulnerabilities identified. Barriers to accessing health services and problems during the cancer journey were also identified [Freeman 2012]. It is known that oncological diseases are among the causes of the highest morbidity and mortality in the world population, in line with the statistics in Brazil, where the incidence has risen annually. This is a motivating factor for health professionals and reference institutions to seek to offer the best care to individuals with cancer, from the diagnostic phase to their end, inferring quality of life throughout the entire trajectory experienced [ANS 2016 and INCA 2023]. Alongside advances in healthcare, when it comes to systematizing care, technology has been accompanying and inserting itself into the sector in order to enable objective, assertive and real-time care. Thus, digital health has been established in the operationalization of services with interdisciplinarity aimed at comprehensive care through the monitoring of patients with relevance in clinical practice [Muniz and Mota and Sousa 2023].

The aim is to shed light on the existence, relevance and functionality of digital health in the oncology navigation service, as a guiding tool in the care developed by health professionals, especially nurses. This study meets one of the Sustainable Development Goals in Brazil proposed by the United Nations, more specifically Health and Well-being and Industry, Innovation, and Infrastructure, with the aim of guaranteeing access to quality healthcare through new scientific knowledge [NUB, 2019].

9.2 The Practice of Patient Navigation

Currently, the patient navigation model has been applied as a proposal for comprehensive and personalized care, which brings benefits to the individual through better prospecting in their journey, being a model of health care in growing expansion, since it is capable of improving and optimizing processes and resources, especially in the oncological area. The need for individualized support at each stage of cancer care is mentioned by Kamei [2023], who reinforces the essential need for the multidisciplinary team to share health information in order for this care to take place. In the Brazilian scenario, patient navigation began in oncology following the model proposed by Harold Freeman, in order to accompany the patient integrally,

with the main focus of accelerating the diagnostic process and the start of treatment, these two points being known to have an impact on the prognosis of the course of the disease [Cavalcante 2013, Pautasso et al., 2018, Freitas Júnior et al., 2021].

Throughout the cancer journey, health professionals, especially nurses, have the opportunity to provide comprehensive and systematized care at all stages of the disease, in order to reduce administrative barriers and favor positive clinical outcomes [De Souza and Fernandes and Veir 2021]. The professional responsible for this systematic and individualized care is called the "navigator", and this role is usually carried out by the nurse, also known as the "nurse navigator". This professional's role includes guiding the patient towards self-care, towards living through the cancer experience, always making use of their expertise and connection with other professionals in the team and sectors that can favor the unfolding of the action [Smith 2014, Shejila and Mamatha and Fernandes 2015]. A Nursing, in the figure of the nurse, has gained prominence in patient monitoring when it comes to coordinating care, where it plays an articulating role between teams, but mainly, acting in the identification of barriers and vulnerabilities inferring care safety and quality of life in the oncological journey [Osório et al., 2021, Borchardt and Sangoi 2022, Vargas et al., 2023].

Through Patient Navigation, there is also a reduction in care costs for the institution, favoring business management and also enabling better allocation of resources, since the needs of individuals are identified and managed early [Silva 2023] Patient satisfaction is also achieved in a more concise manner through this care strategy, which has been gaining notoriety and ascendancy in health services [Borchardt and Sangoi 2022].

In view of the above, cancer navigation services are expanding in the country, offering monitoring during the course of treatment, according to individual needs, focused on the proposed therapy - radiotherapy, surgery, chemotherapy, among other possibilities. In this way, the professional coordinates care by identifying vulnerabilities and/or specific situations for intervention, enabling access, favoring adherence to the therapeutic proposal and the prognosis of the disease [Freeman and Rodrigues 2011, De Lima 2021].

9.3 Technology Allied to Health

It is well known that we are in the century of technology: in addition to computers, cell phones and televisions, artificial intelligence has emerged. These tools provide real-time information on any subject, which used to have to be searched for in one or more libraries, but today is in the palm of our hands. Faced with the new reality of the technological age in health, it has become necessary to talk about health and its relationship with the digital age and consumers. More than 90% of people living with cancer access healthcare information online. Even older people with cancer are also increasingly adopting electronic health services, or eHealth, especially in the pandemic [Verma et al., 2021]. Elderly cancer patients' lack of access to digital technologies is related to barriers such as disadvantaged socioeconomic status, lower levels of education, rapid digital expansion, broadband access, reduced familiarity and frequency of use [Peggy et al., 2022].

As healthcare systems continue to rapidly evolve in terms of incorporating digital health services into patient care, digital health navigation is uniquely positioned to promote health equity and patient-centered care [Offodile and Seitz and Peterson 2021]. Inserted in the digital age, the care managed by the "nurse navigator" takes place in person and also remotely, permeating telenursing, a modality of care with the potential to help the care team, offering support and better working patterns, also breaking cycles associated with adverse events [Mcvey 2023]. They point out that this modality has been used mainly as a way of actively monitoring symptoms in patients undergoing chemotherapy treatment, such as anxiety, depression and fatigue, using specific tools developed by professionals [De Leo et al., 2023].

Telenursing includes activities provided through the use of information and communication technologies combined with telecommunication, leading to an improvement in quality of life, as well as a reduction in emergency and outpatient care, which can also reduce hospitalizations and, consequently, care costs [Kamei 2022]. The monitoring carried out by the professional navigator is based on the premise of favoring the interposition of barriers by individuals, be they financial, cultural, socioeconomic, bureaucratic or psychological, which impact and hinder access to health services [Freeman and Rodrigues 2011].

According to the researchers, the development of technological solutions aimed at early identification and more specific treatments for

cancer also makes it possible to reduce the impact on the individual's daily life [Teixeira et al., 2007]. In this sense, it was noted that the search for health information online seems to be aimed at caregivers and patients seeking a second opinion, such as knowledge of treatment options, shared decision-making and trust in the health system [Verna et al., 2021].

Thus, for this whole process to take place, health professionals and services need to make good use of the tools and technologies available when offering this care to the individual, using not only face-to-face care, but also digital technologies [Kamei 2022]. Given the enormous potential of digital navigation in oncology, it is necessary to apply both change management methodologies and scientific principles of implementation to better guide the lasting insertion of this new role in healthcare [Offodile and Seitz and Peterson 2021].

9.4 Final considerations

Patient navigation requires the use of interactivity in order to monitor the individual and thus meet the premises of the care methodology, which aims to identify and minimize administrative and/or care barriers, monitor treatment and make pertinent referrals during the therapeutic journey, making it essential to use strategies that enable the navigator to be close to the patient. In this way, the digitalization of health is promising, where the use of technology has proved to be an important tool for the development of remote care.

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10 Feasibility of VHEE-FLASH Radiotherapy in Hypoxic Tumors

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Abstract

The proliferation of tumor mass in solid tumors leads to structural anomalies in tumor vasculature, resulting in a state of hypoxia. The low oxygen concentration in these tumors makes them resistant to radiation in radiotherapy. FLASH radiotherapy, with ultra-high dose rates, aims to reduce toxicity in adjacent tissues while maintaining treatment quality. Among the various potential future implementations of FLASH radiotherapy, the use of Very High Energy Electrons (VHEE) with energies ranging from 50 to 250 MeV stands out. Computational simulation is crucial for exploring dosimetric properties in tissues with varying oxygen concentrations or hypoxic scenarios. Therefore, this research aims to investigate the dosimetric properties of VHEE-FLASH radiotherapy in tumors with low oxygen concentrations through Monte Carlo simulations implemented with the TOPAS code. To achieve the objectives of this study, eight tumors with distinct oxygen fractions, each characterized by varied densities and specific associations with O_2 pressures, were simulated and positioned at the center of a cylindrical geometry simulating the anatomy of an adult head. In the simulation, 10^8 primary particles were employed in a VHEE beam with a Gaussian distribution of 250 ± 0.75 MeV. The results showed a direct correlation between the increase in oxygen pressure and the dose deposited in tumors, analogous to patterns noted in the literature concerning the behavior of photon beams. A linear increase in energy deposition was observed as oxygen pressure exceeded hypoxic values. The analysis of the dose profile perpendicular to the radiation axis showed a 5.44% difference in the maximum dose between hypoxic and normoxic tumors. Our results indicate that the VHEE electron beam is a strong candidate for tumor treatment under FLASH conditions (> 40 Gy/s), exhibiting the anticipated oxygen enhancement effect of this technique.

Keywords: VHEE; FLASH Radiotherapy; Hypoxic tumor.

Sustainable Development Goals (SDG): 3. Good Health and Well being; 9. Industry, Innovation, and Infrastructure.

10.1 General Information

The success of radiotherapy treatment is associated with the dose delivered to the tumor, limited by the tolerance of toxicity in healthy tissues near the irradiated area (BARNETT et al., 2009). In this context, FLASH radiotherapy, based on ultra-high dose delivery rates (> 40 Gy/s) and rapid (< 200 ms) treatments, has emerged as one of the most promising proposals for cancer treatment in recent years, providing a reduction in side effects associated with conventional radiotherapy (LIU et al., 2023; KACEM et al., 2022), especially to decrease radiation-induced toxicity in healthy tissues without compromising the quality of tumor control (FAVAUDON et al., 2014). The reduction of toxicity in these tissues is referred to as the FLASH effect. One of the main hypotheses explaining the mechanism of the FLASH effect is oxygen depletion, which occurs when healthy tissue is exposed to an ultra-high dose delivery rate, leading to rapid local oxygen depletion and rendering the tissue radioresistant to ionizing radiation (DURANTE, BRÄUER-KRISCH, HILL, 2018). In this sense, FLASH radiotherapy can reduce the production of reactive oxygen species, diminishing the generation of indirect damage from ionizing radiation in healthy tissues (SPITZ et al., 2019).

Highly energetic electron radiotherapy (Very High Energy Electrons - VHEE), with energies ranging from 50 to 250 MeV, began to be investigated in the early 2000s and has demonstrated precision while being minimally affected by tissue heterogeneities, making it suitable for deep-seated tumors (DESROSIERS et al., 2000; LAGZDA et al., 2020; PAPIEZ L., DESROSIERS and MOSKVIN, 2002). Although commercial VHEE equipment is not yet available, linear accelerators with acceleration gradients greater than conventional ones are being produced for this purpose (WU et al., 2021). Furthermore, the use of Laser Wakefield Accelerators (LWFA) operating at high repetition rates, in the order of several tens of kHz, is an alternative for implementing FLASH radiotherapy (DOSANJH et al., 2020). In an LWFA, as a high-intensity laser pulse propagates through a plasma, it disturbs its electrons. This disturbance gives rise to a high-amplitude electric field in the wake of the laser pulse, known as the 'wakefield,' which can be utilized to accelerate plasma electrons to energies on the order of a few GeV in just a few centimeters of propagation (GONSALVES et al., 2019). Given that the acceleration gradients supported by an LWFA are orders of magnitude higher than those provided by radiofrequency-based technology accelerators, the use of this technology may result in the development of

compact and cost-effective accelerators capable of delivering high-energy electron beams (SHALLOO et al., 2020).

Currently, computational studies play a crucial role in enabling the manipulation of relevant parameters, providing a deeper understanding of radiation dose deposition in different oncological contexts. As part of this evolution, the National Cancer Institute in the United States launched an initiative that led to the development of TOPAS, an open-source code capable of simulating the interaction of energetic particles with various materials using the Monte Carlo method (FADDEGON et al., 2020). In this context, the application of TOPAS emerges as a viable alternative to deepen the understanding of dosimetric properties in hypoxic tumors undergoing the FLASH radiotherapy modality, associated with the use of VHEE beams generated by LWFA. Thus, a specific dosimetric study in hypoxic tumors allows us to understand how FLASH-VHEE radiotherapy interacts and influences the radiobiological behavior of these tumors. Therefore, this study aims to investigate the dosimetric properties of FLASH-VHEE radiotherapy in tumors with low oxygen concentrations using the TOPAS code. The TOPAS-Monte Carlo code can be utilized to investigate dosimetric properties in hypoxic tumors undergoing FLASH-VHEE radiotherapy. Therefore, the primary emphasis of this chapter is to examine properties in low-oxygen tumors using VHEE beams to establish a FLASH-VHEE radiotherapy technique, employing TOPAS.

10.2 Methods

Monte Carlo simulations in this study were facilitated by the TOPAS code version 3.9, allowing the creation of various materials by defining the chemical composition of elements, the mass fraction of each element, density, and average excitation energy. It also includes predefined materials (FADDEGON et al., 2020), such as healthy tissues (WENGER et al., 2015), based on the existing soft tissue in the Geant4 material database, referred to as G4_TISSUE_SOFT_ICRP (ALLISON et al., 2006; ALLISON et al., 2016; GUATELLI et al., 2011). By adjusting the oxygen mass fraction, we created eight tumors, each characterized by different densities and associations with O₂ pressures (FADDEGON et al., 2020; WENGER et al., 2015; ALLISON et al., 2006; ALLISON et al., 2016; GUATELLI et al., 2011). Equation (1) Dalton's Law was applied to determine the oxygen pressure associated with a concentration or mass fraction of this element (WENGER et al., 2015),

$$pO_2(mmHg) = pO_2(\%)p_{atm} \quad (1)$$

where $pO_2(mmHg)$ represents the oxygen (O_2) pressure in mmHg, $pO_2(\%)$ represents the mass fraction of oxygen, and p_{atm} refers to atmospheric pressure in water, which is equivalent to 760 mmHg. In addition, the individual densities of each tumor were calculated using Equation (2):

$$d_1 = \frac{\sum_{i=1}^n f_{1,i}m_i}{\sum_{j=1}^n f_{0,j}m_j} d_0 \quad (2)$$

where $f_{0,j}$ and m_j denote, respectively, the (original) mass fraction and atomic mass of the j -th element constituting soft tissue, and $f_{1,i}$ and m_i represent the (altered to represent the desired composition of the tumor) mass fraction and atomic mass of the i -th element constituting tumor tissue. Additionally, d_0 is the density of soft tissue (1 g/cm^3). Geant4 calculations include details from the material database regarding soft tissue composition and the mass fractions of each component. Given the similarity in mass fractions of other elements between soft tissue and tumor tissues, normalization of tumor compositions with modified O_2 mass fractions was automatically performed by TOPAS. This was achieved by activating the parameter *NormalizeFractions* = *True*, ensuring that the total mass fraction of all elements sums to unity. (PERL et al., 2012; ALLISON et al., 2006; ALLISON et al., 2016; GUATELLI et al., 2011).

The oxygen concentrations in the simulated tumors range from 0.01% to 21.00%, corresponding to an oxygen pressure range of 0.076 mmHg to 160 mmHg. While 21% oxygen fractions indicate normoxic conditions, concentrations of 3%, 9%, and 15% represent physioxia. Finally, fractions between 0.01% and 1% indicate hypoxic states (MCKEOWN, 2014). Table 1 presents the simulated conditions for oxygen fractions and tumor densities used.

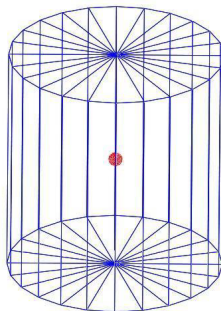
Table 1. Simulated conditions of pO₂ and tumor density.

Tumor	pO ₂ (%)	pO ₂ (mmHg)	Density (g/cm ³)
1	0.01	0.076	0.296
2	0.1	0.76	0.297
3	1.0	7.6	0.302
4	3.0	22	0.308
5	5.0	38	0.332
6	9.0	68	0.405
7	15.0	114	0.479
8	21.0	160	0.552

To investigate the response of simulated tumors to different oxygen pressure levels, a cylindrical soft tissue geometry with a diameter of 18 cm and height of 20 cm was created, representing the anatomy of an adult head. In this model, spherical tumors with a diameter of 1.1 cm were positioned at the center of the simulated geometry. These tumor dimensions are representative of the dimensions of a glioblastoma (URBÁNSKA et al., 2014).

In the simulation scenario, 10⁸ primary particles were used in a VHEE beam, with Gaussian distributions in space ($\sigma_x = \sigma_y = 6.5$ mm), an average kinetic energy $E_k = 250$ MeV, and energy spread $\sigma_{E_k} = 0.75$ MeV. The beam had a 3.2 mrad angular deviation in x and y for irradiating tumors with different oxygen pressures (WHITMORE et al., 2021). The distance between the radiation source and the cylindrical phantom is 100 cm, and the irradiation field used has dimensions of 1.5 x 1.5 cm². Additionally, the beam impinges parallel to the Z-axis, reaching the upper part of the cylinder. Figure 1 illustrates the arrangement of the simulated structures.

Figure 1. Illustration of the geometry used in TOPAS.



The simulation results were analyzed considering the energy and dose deposited in the tumor volumes for a single shot of the simulated beam. For evaluation, a detector was simulated in the parallel world, positioned at the center of the tumor region, sized at $1.2 \times 1.2 \times 1.2 \text{ cm}^3$, and subdivided into 100 bins along the x , y , and z axes. Energy deposition detection was performed using the *EnergyDeposited scorer*, which calculates the sum of energies deposited in the tumor volume. Meanwhile, the detection of the accumulated dose was achieved using the *DoseToMedium scorer*, which calculates the sum of energies deposited divided by the tumor mass. Additionally, the *g4em-penelope* physics module was employed. This physics module is based on the list of physical processes called *G4EmPenelopePhysics* in Geant4, specifying the particles and physical processes used in the simulation.

To examine the oxygen effect on dose distribution in tumors with different levels of oxygen pressure, dose profiles and dose distributions along the x and y axes were compared for tumors with oxygen pressures of 0.076 mmHg and 160 mmHg. The output type, specified in the TOPAS script, consisted of CSV (comma-separated values) files. For data analysis and post-processing, the Python programming language was used.

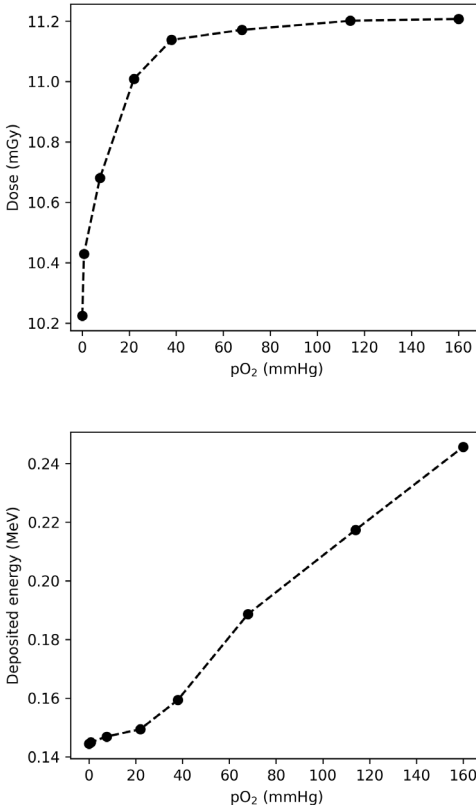
The Oxygen Enhancement Ratio (OER) is a crucial parameter in radiobiology used to quantify the impact of the presence of oxygen on the efficacy of radiation. The OER values associated with each oxygen pressure used in the simulations were calculated by applying Equation (3), which quantifies the relative radiation sensitivity at a specific oxygen pressure (pO_2 (mmHg)) compared to the sensitivity in the hypoxic state at a defined isoequivalent level (KIRKPATRICK, CARDENAS-NAVIA and DEWHIRST, 2004).

$$OER = \frac{1 + 0.81pO_2^{0.616}}{1 + 0.324pO_2^{0.616}} \quad (3)$$

10.3 Results and Discussion

The analysis of results from simulations conducted for various oxygen pressures demonstrates that the increase in oxygen pressure is directly correlated with an increase in deposited dose, accompanied by a simultaneous intensification of radiosensitivity in the tumor volume, as depicted in Figure 2 (left).

Figure 2. Deposited dose (left) and energy deposited (right) for eight tumors with different O_2 pressures (mmHg).

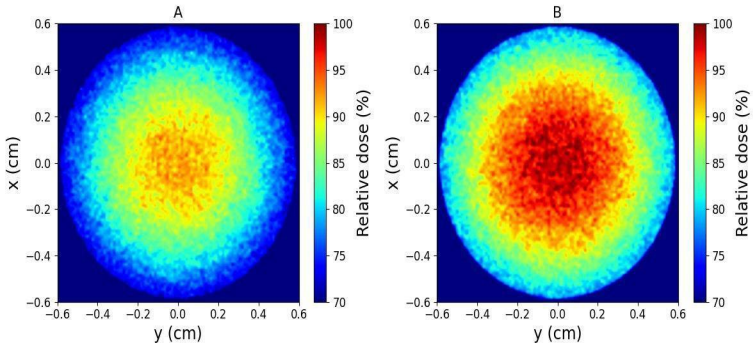


This relationship demonstrates that as the pressure and oxygen fraction in the tumor volume increase, tumors exhibit a progressive and heightened sensitivity to radiation. This observed behavior persists until reaching a pressure of 160 mmHg, characterized by normoxia, which is the normal oxygen level for cells in soft tissue (HALL and GIACCIA, 2006). Additionally, a notable increase in deposited dose and, consequently, in radiosensitivity is highlighted, especially between pressures of 0 and 38 mmHg, corresponding to oxygen fractions ranging from 0.01% to 5%, which

is a region between hypoxic and physioxic states. The maximum difference found in absorbed dose values occurs between pressures of 0.076 mmHg and 160 mmHg, with an increase in absorbed dose of 9.8% in the study scenarios of this work. Figure 2 (right) also shows an almost linear increase in energy deposition as the oxygen pressure exceeds 40 mmHg. In this context, as the oxygen concentration in tumors increases, there is a corresponding increase in the energy deposited by the incident particles in the tumor volume. These results are in agreement with findings previously documented in the scientific literature (ALVA-SÁNCHEZ and PIANOSCHI, 2020; TAYLOR, HILL and LÉTOURNEAU, 2022). The observation of this linear increase in deposited energy with oxygen pressure can be attributed to the greater efficiency of the energy deposition process when oxygen pressures are close to normoxic conditions.

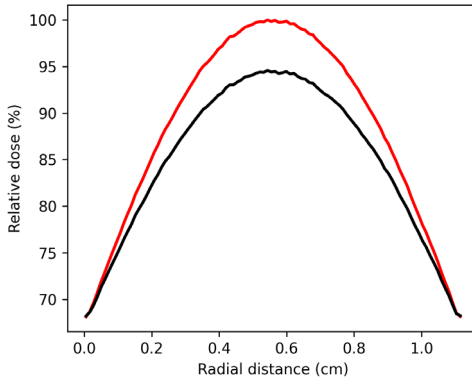
Figure 3 represents the dose distribution in simulated tumor volumes, all with a diameter of 1.1 cm, subjected to different combinations of pressures and fractions of oxygen. Under conditions of tumor normoxia (160 mmHg and 21% O₂), a significant increase in the dose percentage is observed not only in the central region of the tumors but also in their adjacent areas, compared to the dose distribution corresponding to a tumor in a hypoxic state (0.076 mmHg and 0.01% O₂). The explanation for this disparity lies in the effects of oxygenation on the phenomenon of radiosensitivity. Under normoxic conditions, tumor cells demonstrate greater sensitivity to radiation. The increased dose concentration in the central region and surrounding areas of the tumor volume during normoxia can be attributed to the differentiated biological response of tumor cells to more favorable oxygenation conditions. In contrast, under hypoxic conditions, simulated tumor volumes show lower sensitivity to radiation due to oxygen deficiency, resulting in a less concentrated dose distribution in the central and adjacent regions of the tumor. Notably, outside the region of interest, it is observed that the dose distributions are similar in both cases, with dose percentages close to 70%.

Figure 3. Dose distribution in tumors: (A) tumor in a hypoxic state $pO_2(\%) = 0.01$ and $pO_2(\text{mmHg}) = 0.0076$; (B) tumor in a normoxic state $pO_2(\%) = 21.00$ and $pO_2(\text{mmHg}) = 160$.



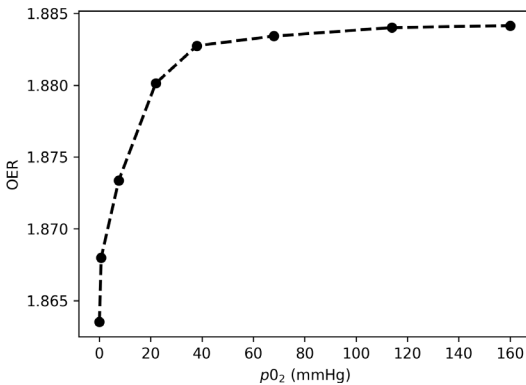
This difference between the doses in tumors in a hypoxic and normoxic state becomes evident when analyzing the dose profile perpendicular to the irradiation axis in tumors, as shown in Figure 4. The results reveal a 5.44% difference in the maximum dose between tumors at a radial distance of 0.6 cm.

Figure 4. Dose profile of tumors in a hypoxic and normoxic state.



The OER values associated with each oxygen pressure used in the simulations are graphically represented in Figure 5. An upward progression in OER values is observed until reaching 60 mmHg. Subsequently, the OER relative to the absorbed doses at each oxygen pressure used shows a tendency to stabilize at a constant value. This pattern of behavior highlights increased efficacy in inducing biological effects as the oxygen fraction in the tumor volume and O_2 pressure increase until these factors reach a constant condition in the normoxic state. This behavior, along with the conformity of the curve shape in the relationship between OER and the oxygen pressure used, is in agreement with results found in the literature (KIRKPATRICK, CARDENAS-NAVIA and DEWHIRST, 2004; ALVA-SÁNCHEZ and PIANOSCHI, 2020; GRIMES and PARTRIDGE, 2015).

Figure 5. Relative OER for each tumor with different O_2 pressures.



10.4 Conclusion

The study investigated the dosimetric properties of FLASH-VHEE radiotherapy in simulated tumors with different levels of oxygen pressure and fraction. Using Monte Carlo simulations with the TOPAS code, eight tumor scenarios representative of hypoxic, physioxic, and normoxic conditions were created. The results showed a direct correlation between the increase in oxygen pressure and the deposited dose in tumors, indicating increased radiation sensitivity under normoxic conditions. A linear increase in energy deposition was observed as oxygen pressure

exceeded hypoxic values, suggesting increasing efficacy of the energy deposition process under normoxic conditions. The dose distribution in tumors revealed a significant concentration in the central region under normoxic conditions, in contrast to a less concentrated distribution under hypoxic conditions. Analysis of the dose profile perpendicular to the irradiation axis showed a 5.44% difference in the maximum dose between hypoxic and normoxic tumors. Additionally, the OER highlighted the influence of oxygen presence on radiation efficacy, demonstrating increased sensitivity under normoxic conditions. Considering the results obtained in this work, a VHEE electron beam with the adopted parameters has a total charge of approximately 16 pC and deposited a dose of approximately 10 mGy in the hypoxic tumor. Thus, to achieve the dose rates required for observing the FLASH effect, it would be necessary to provide electron beams with the described parameters at a repetition rate equal to or greater than 4 kHz. Despite the unavailability of commercial clinical accelerators capable of meeting these requirements, the constant advancement of laser and LWFA technologies may enable the achievement of the FLASH effect via VHEE radiotherapy based on laser-plasma interactions in the near future.

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11 Navigating Healthcare Innovation: The Role of Probabilistic Networks in Advancing Clinical Decision Support Systems

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Abstract:

This chapter aims to present the research conducted on the development of Clinical Decision Support Systems (CDSS), based on probabilistic networks, by students and faculty affiliated with the CNPq research group, named DISTANCE EDUCATION IN HEALTH EDUCATION. The CDSSs were constructed using the SR-Bayes framework, also developed by researchers within the research group. The Clinical Decision Support Systems developed cover the following areas: Oncological Physiotherapy, Risk of Laryngotracheal Aspiration, and Decision Support System for Caregivers of Pediatric Hemophilic Patients. The systems have been evaluated by domain experts; however, before being made available to end users, they need to undergo a knowledge base validation process to ensure an adequate level of reliability, accuracy, and precision in the analysis of available data and the recommendations provided.

Keywords: Clinical Decision Support Systems, Probabilistic Networks, SR-Bayes.

Sustainable Development Goals (SDG): Health and well-being, Quality Education.

11.1 General Information

With all the technological changes and health practice developments already identified in the 21st century, the development of Decision Support Systems applied in the healthcare sector emerges as a particularly necessary technology. This need is driven by the increasing challenges related to information and knowledge management in healthcare, the growing adoption of electronic medical record systems, and the desire to offer personalized healthcare services tailored to each patient's situation and preferences [Musen, Middleton and Greenes 2021].

Clinical Decision Support Systems (CDSS) can be defined as programs designed to directly assist in clinical decision-making, where individual patient characteristics are combined with a computerized clinical knowledge base. The information is then presented to the medical team or the patient through alerts or recommendations to aid in the decision-making process [Sim et al. 2001]. However, according to some authors, the focus in recent decades has shifted to the development of tools providing specific recommendations for the patient, known as advanced CDSS. These systems would include, for example, checking medication interactions and diseases, supporting individualized dosage during treatment, or providing recommendations on laboratory tests [Wasylewicz and Scheepers-Hoeks 2019].

Like any innovation in healthcare, CDSS undergoes a rigorous evaluation process before being made available to end users [Shahsavarani et al. 2015], ensuring an adequate level of reliability, accuracy, and precision in the analysis of available data and offered recommendations. It is expected, therefore, that the use of CDSS will lead to improvements in patient safety and care quality, treatment outcomes, and a reduction in reliance on memory, error rates, and response times [Beeler, Bates and Hug 2014].

Time limitations, the time spent by professionals with patients, and constantly evolving healthcare standards contribute to errors and delayed clinical decisions. Errors are primarily related to inadequate time for patient assessment, resulting in less precise diagnoses, prioritization of less relevant clinical data, or failure to recognize complications and urgent situations [Castaneda et al. 2015].

Many studies confirm the effectiveness of CDSS based on probabilistic network applications. This technology is ideal for handling uncertainty, common in healthcare, and is capable of intuitively modeling

domain expert knowledge [Flores et al. 2000].

This chapter aims to present the SR-Bayes framework [Oliveira 2019], developed to assist in the implementation of Clinical Decision Support Systems. The Decision Support Systems built from SR-Bayes by students and faculty affiliated with the CNPq research group, called Distance Education in Health Education, will be discussed [Bykowski 2019] [Alonso 2022] [Bauermann 2023].

11.2 Probabilistic Networks

People solve problems and make decisions in environments where information is partial (i.e., not complete) or approximate (i.e., not exact). Attempts have been made to emulate this capability in intelligent systems, but for problems formulated with partial or approximate information, only approximate solutions can be obtained, meaning with uncertainty. Therefore, it becomes necessary to have ways to deal with uncertainty. In the late 1980s, there was a renewed interest in probabilistic approaches to handle uncertainty, motivated by the discovery that by considering the causal relationship and (conditional) independence between variables in the domain, it is only necessary to represent conditional probabilities between directly dependent variables (rather than all variables), making this representation computationally manageable. This resurgence is associated with the emergence of probabilistic networks, i.e., models based on graphical representations of the probabilistic dependencies in the application domain. The use of these networks has the following characteristics: a) allows for representing and manipulating uncertainty based on well-founded mathematical principles, b) models domain expert knowledge in an intuitive way, and c) is the only formalism that allows performing any of the possible types of probabilistic inference, i.e., causal, diagnostic, intercausal, or mixed. Bayesian Networks (BN), Markov Networks (MN), and Influence Diagrams (ID) are probabilistic networks.

A BN is a directed acyclic graph, where nodes represent random variables, and the arc connecting two nodes represents the probabilistic dependence between the associated variables. Each node stores the conditional probability distribution function of the values that the random variable associated with the node can take, given the values of its parent nodes (i.e., those directly linked to the node in question). Figure 1 shows an illustrative example of a BN. From a Bayesian network, an equivalent Markov network can be constructed (a similar acyclic graph but without

directed arcs). Both are compact representations of the joint probability distribution function of all random variables in the modeled domain. The main feature of probabilistic networks is the ability to explore the graph structure and reduce the calculation (of the conditional probability of an event given the available evidence) to a series of local calculations, using only variables obtained from a node and its neighbors in a graph structure, avoiding the computation of the global joint probability distribution function. The graphical representation also explicitly shows dependency relationships and constitutes a powerful tool in knowledge acquisition and verification processes [Jensen 2009].

Figure 1. Illustrative example of a BN, where the conditional probability distribution function of a node labeled “Fall Prevention” is represented by a Conditional Probability Table (CPT). The CPT of this node incorporates the states of its parent nodes “Age” and “History of Falls”.



11.3 Bayesian Recommendation System in Health (SR-BayeS)

With the widespread adoption of the Internet through mobile devices, a branch of electronic health has emerged, known and disseminated as mobile health (mHealth). This facilitates continuous assessment of health parameters, introduces a new environment for promoting healthy behaviors, and aids in the self-management of chronic conditions, among other applications. This field involves the use of biosensors, implantable devices, power supplies, wireless communication networks, processing units, user interfaces, software, and algorithms [Rocha et al. 2016] [Pereira Neto and Flynn 2019]. Among the main categories of mobile health, the development of systems to support decision-making [Kay, Santos and Takane 2011] [Rocha et al. 2016] stands out.

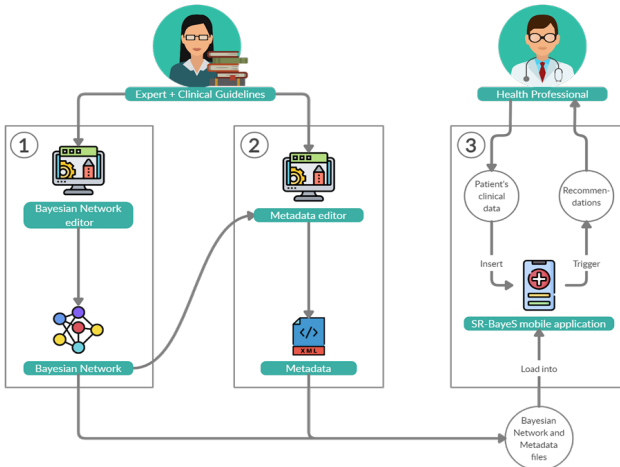
A research group comprised of students and faculty from the Federal University of Rio Grande do Sul (UFRGS) and the Federal University of Health Sciences of Porto Alegre (UFCSPA) identified that, due to the need of knowledge and technical software development skills, projects developed

by healthcare experts were at great risk of being limited to the theoretical sphere [Oliveira 2019]. Consequently, without the development of a prototype, many of these projects end up being archived without offering the benefits originally planned for their target audiences. To minimize this risk, researchers developed the Bayesian Health Recommendation System (SR-BayeS).

The SR-BayeS framework is designed to facilitate the implementation of Clinical Decision Support Systems developed by healthcare professionals within a mobile application capable of operating effectively in real-world scenarios involving uncertainty [Oliveira 2019].

The design and use of a CDSS through SR-BayeS happens through three stages, as shown in Figure 2. The three stages can be divided into two parts: knowledge base modeling by the expert, represented by stages 1 and 2, and the system's use by the Health Professional, represented by stage 3. The knowledge base required for the CDSS to function in SR-BayeS consists of two parts: the Bayesian network (BN) and the system metadata. In general, the BN is the inference mechanism, constituting the logical part of the system, and the metadata contains information defining the assembly of the presentation structure, constituting the user interaction interface part of the system.

Figure 2. Stages of construction and use of a Clinical Decision Support System using the SR-BayeS framework Source.



Stage 1 refers to the creation of the BN by the expert. The construction of a Bayesian network typically involves the following steps: Identification of relevant variables, determining which variables are involved in the problem; Specification of dependencies, determining the probabilistic dependencies between identified variables, which can be done through literature reviews, expert interviews, and data analysis; Network structure, where a directed acyclic graph is constructed representing the identified probabilistic dependencies, composed of nodes representing variables and edges representing probabilistic dependencies; Probability assignment, where a probability distribution is assigned to each variable based on available information, such as historical data, case studies, or clinical experience; Network consistency check, i.e., whether the probabilities assigned to each variable are consistent with the specified probabilistic dependencies in the network; Sensitivity analysis, testing the network's robustness by conducting sensitivity analyses to determine how uncertainties in probability distributions affect conclusions derived from the network; and Network validation by comparing its predictions with real data or other independent sources of information. These steps can be repeated to enhance and refine the Bayesian network over time. The process of building a Bayesian network is iterative and requires collaboration from experts in different areas of knowledge [Druzdzel and Van der Gaag 2000]. Specialized software exists for building and editing BNs, such as Hugin [Madsen et al 2003] [Jensen 2009], used in the development of this framework.

Stage 2 refers to the creation of metadata by the expert. Armed with the BN in .net file format, the expert can load it into a desktop application for Windows called the SR-BayeS Metadata Builder. This application allows the classification of variables from the BN into evidence insertion and recommendation, essential information for the system's operation, and the association of evidence variables with predefined patient registration information, such as age or gender. Based on classification and association, the application exports a .xml file with the metadata necessary for the immediate application of the system. Further customization is possible through XML file adjustments, including creating different types of questions and detailing recommendations displayed with text and/or images [Oliveira 2019].

With the BN and metadata defined, the mobile application named SR-BayeS installed on an Android smartphone generates the CDSS, optionally

complemented by a .zip file containing images and PDF files. Through the SR-Bayes interface, these files can be loaded into the system. This procedure is only necessary on the first use [Oliveira 2019].

To use the system, the user must install the application on a mobile device with the Android operating system. With the metadata loaded into the system, the user can use the Clinical Decision Support System by registering a new patient or using a previously registered patient and inserting evidence. Recommendations will be displayed after or, optionally, during the insertion of evidence, and the user can access their details at any time, with these being saved in the application's internal database [Oliveira 2019].

11.4 Applications and Results

In this section, three applications of SR-Bayes are described.

11.4.1 Oncological Physiotherapy

Increased survival of cancer patients presents new challenges in terms of demand volume and management complexity. To advance the process of functional oncological rehabilitation, a functional physical evaluation was utilized as the basis for developing a clinical decision support system for cancer rehabilitation. The objective of this study was to develop a decision support system for the recommendation of appropriate physiotherapeutic procedures for the rehabilitation of hospitalized cancer patients, which simulates the opinion of a specialist in the field [Bykowski 2019].

This is a methodological study, which presents all the steps of building a clinical decision support system, created through a Bayesian health recommendation system. The steps include modeling expert knowledge, modeling the system interface and the system on the mobile device. The theoretical support was based on the model of functional physical assessment in oncology, a physiotherapeutic assessment book, oncology manuals, patient guidance manuals, and scientific articles. This specialized domain knowledge was important for the generalization of the predictive model and the implementation of a Clinical Decision Support System. Therefore, scientific literature focused on the assessment and physiotherapeutic treatment of oncology patients was adopted to be modeled in a Bayesian Network (BN). In addition, the study included the evaluation of the system by specialists to analyze the technical quality of

the recommendations and the functionality of the system, and an automated evaluation of 170 cases from the database, where there was automatic insertion of clinical data into the system, simulating its use by a professional. The database was obtained through a partnership with Santa Casa de Misericórdia of Porto Alegre, approved by the Ethics Committee of this institution (CAEE: 95981618.7.0000.5335).

Through the evaluation of the technical quality of the recommendations, we found a great predominance of total agreement with the recommendations triggered by the system (79% of the answers) and by the evaluation of the functionality, we observed more reports of the need for adjustments in the system (55% of the answers), mainly focused at the insertion of clinical data and the need for operational guidelines for the correct handling of the system. The results produced by the automated evaluation pointed to a greater number of recommendations triggered by the system in comparison to the number of physiotherapeutic conducts described in the electronic patient records. The total of recommendations triggered by the system (totaling all levels of recommendation probability) was 1.144, while the total number of effectively evolved medical records (for all levels of likelihood of recommendation) was 565. In relation to this aspect, it is essential to reinforce the concept for which the CDSS was designed and structured to guide the initial steps of therapeutic approach development. This implies that the recommendations resulting from the processing of the BN are more comprehensive, aiming to support physiotherapy students in their training rather than those recorded in day-to-day electronic medical records.

We understand that the use of the clinical decision support system for cancer rehabilitation is feasible and promising for the qualification of patient care. The results generated, from the evaluations, indicate a compatibility between the human reasoning and the algorithm, which reinforces the possibility of its implementation. Its use assists the professional in the face of the complexity that involves the oncologic patient, making possible the individualization and adaptation of the rehabilitation in a hospital environment.

11.4.2 Risk of Laryngotracheal Aspiration

Screening for the risk of laryngotracheal aspiration in hospitalized adults is a complex and interdisciplinary task that involves multiple variables and causes. The objective of this study was to develop and assess

the applicability of a clinical decision support system based on Bayesian Network to assist the interdisciplinary hospital team, called SR.REAL [Alonso 2022].

A Bayesian network was constructed using a systematic literature review to identify and categorize the main variables required for assessing the risk of laryngotracheal aspiration. These variables were grouped into the patient's current diagnosis, history of swallowing disorders, swallowing-related aspects, and basic epidemiological characteristics. It was considered for the analysis and quantitative development of a database with 232 real clinical cases. The database was obtained through a partnership with Santa Casa de Misericórdia of Porto Alegre, approved by the Ethics Committee of this institution (CAEE: 44920121.0.0000.5345). These patients were clinically evaluated with the Gugging Swallowing Screen (GUSS) scale [Park, Kim and Lee 2020]. It is important to emphasize that the clinical evaluation of swallowing is another standard for diagnosing dysphagia and understanding the risk of laryngotracheal aspiration. Four risk levels were defined for the system: high risk 55.01% to 100%; moderate risk 30.01% - 55%; low risk 5.01% - 30% and minimum risk 0% -5%. These criteria are defined in the Manchester protocol [Cooke and Jinks 1999] and adapted by the experts who developed this Bayesian network.

The system was evaluated by a group of specialists (n=9) from various disciplines including physicians, nurses, nutritionists, and speech pathologists, following the guidelines of ISO/IEC 25010, 2011 [ISO 2011]. This standard is a reference for promoting the performance of the internal and external quality of software products. It is based on three levels: features, sub-features, and metrics.. The specialists considered the software product to be functional (86.1%), reliable (83.3%), usable (84.4%), efficient (92.6%), maintainable (90.4%), and portable (88.9%).

The interdisciplinary screening system developed in this study was found to be valuable and feasible for use by specialists.

11.4.3 Decision Support System for Caregivers of Pediatric Hemophilic Patients

Hemophilia, a rare disease characterized by blood clotting factors deficiency, is diagnosed in the first years of patients' lives. Therefore, their caregivers must be trained to manage the disease. Considering this, information technologies represent a promising alternative to expanding access to information and improving health services. The objective of this

study was to develop an application with a Clinical Decision Support System and digital Infusion Log Diary, called HemoAssist, to assist caregivers of children with hemophilia [Bauermann 2023].

The development of HemoAssist was carried out in three phases: 1. Identification of risk indicators for bleeding episodes and recommendations for managing the disease; 2: Development of the Clinical Decision Support System (CDSS) using Bayesian Networks and the digital version of the Infusion Log Diary; 3: Assessment of the relevance of the application's content through a survey with experts.

The system was evaluated by a group of specialists (n=5) The system was evaluated by a group of specialists (n=5) using the Instrument for Validation of Health Educational Content (IVHEC), which comprises three domains: objectives, structure and presentation, and relevance [Leite et al., 2018]. According to the experts, the HemoAssist application covers a relevant theme (100%), addresses the proposed topic (100%), encourages reflection on the issue (100%), encourages behavior change (100%), presents correct (100%) and necessary (100%) information, and offers appropriate language to the educational material (100%). Furthermore, the application is suitable for the teaching-learning process (67%), clarifies questions about the topic (67%), offers objective (67%) and clarifying information (67%), with a logical sequence of ideas (67%) and text with an appropriate font size (67%). Regarding the adequate language for the target audience, there was a consensus that there is still an opportunity for improvement (100%).

This study corroborates the benefits and need for a software application that brings together, in a single place, various information that is useful and easy to access and understand for caregivers of children with hemophilia.

11.5 Conclusion

The projects developed using the SR-Bayes framework reveal their innovative and interdisciplinary nature. The SADCs have been evaluated by domain experts; however, before being made available to end users, they need to undergo a rigorous evaluation process, ensuring an adequate level of reliability, accuracy, and precision in the analysis of available data and the recommendations provided.

Among the 17 Sustainable Development Goals established by the United Nations (UN) in 2012 to address the greatest challenges of our time,

care for the planet, and improve the lives of all, our research group highlights: the goal of HEALTH AND WELL-BEING. The clinical decision support systems developed aim to provide accurate clinical information to patients and/or caregivers through the HemoAssist APP, remotely bringing health to those who need it most. Additionally, the group emphasizes the goal of QUALITY EDUCATION, as the SR-Bayes Oncological Rehabilitation and SR.REAL APPs seek to assist the interdisciplinary hospital team, which also includes professionals in training, in their daily decisions alongside their inpatients.

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12 Application of Mathematical Models in the Assessment of Radiobiological Parameters in Radiotherapeutic Treatments for Prostate Cancer

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Abstract:

Most cancer patients undergo curative therapies, with radiotherapy being the most common. The assessment of radiotherapeutic planning occurs through the DVH, which analyzes the dose in the volume of interest without considering biological parameters. Mathematical models, such as TCP (Tumor Control Probability) and NTCP (Normal Tissue Complication Probability), consider radiobiological parameters, predicting the fraction of surviving tumor cells as a function of radiation dose and the complication of adjacent tissues. Through TCP, it is possible to measure the effectiveness of a treatment, allowing for protocol comparisons, while NTCP analyzes complications in adjacent tissues. Thus, this chapter analyzes different parameters for TCP and NTCP models.

Keywords: Radiobiology; Mathematical models; Prostate cancer; Radiotherapy.

Sustainable Development Goals (SDG): This research aligns with the Sustainable Development Goals (SDGs) by addressing SDG 3: Good Health and Well-being and SDG 9: Industry, Innovation, and Infrastructure, supporting advancements in healthcare and fostering improvements in cancer therapy.

12.1 Introduction

Cancer can be defined as the disordered and uncontrolled growth of cells during cell division and can affect any region of the body. This growth may occur due to internal factors such as hormonal imbalance, immunological conditions, hereditary factors, or external factors such as ionizing radiation, which can cause DNA breakage and consequently the proliferation of defective cells [Naoum and Naoum 2016].

According to the National Cancer Institute (2023), cancer is the leading public health problem worldwide and ranks among the top four causes of death before the age of 70 in most countries. In 2020 alone, there were approximately 19 million new cases. Following lung cancer, prostate cancer is the second most common cancer in men, accounting for about 14.1% of cases. Iser *et al* report that the incidence of this cancer is 30.7 cases per 100,000 inhabitants. In Brazil, more than 18,000 deaths from this disease were recorded in 2020.

To extend the life expectancy of patients affected by prostate cancer, early diagnosis of the disease and prompt initiation of treatment are crucial. The treatment of this type of neoplasm may involve the use of three treatment techniques: prostatectomy, radiotherapy, and chemotherapy [Sousa *et al* 2019]. Currently, it is known that radiotherapy is the most frequently used treatment for patients with prostate cancer, and other types of treatment are more indicated in cases where the disease has progressed, meaning that radiotherapy is widely used in patients with localized prostate cancer [Chimin 2020].

Radiotherapy uses ionizing radiation to destroy tumor cells and prevent their spread, while protecting nearby healthy tissues. It involves high-energy radiation from radioisotopes (brachytherapy) or a linear accelerator (teletherapy) [Brum *et al* 2020]. For prostate cancer, treatment typically includes daily doses of 1.8 to 2.0 Gy over 35 to 44 fractions, depending on the clinical protocol [AMB 2021]. This method aims to maximize therapeutic effectiveness and minimize side effects, with dose and fractionation tailored to individual patient needs.

In radiotherapeutic treatment, dose control is essential for preserving healthy tissue adjacent to the tumor volume. Overdosing on healthy tissues can lead to unwanted side effects, such as the development of secondary cancer due to radiation. Furthermore, dose control is necessary to ensure treatment effectiveness. Therefore, radiotherapy protocols are established to prescribe dose uniformity in the target [International Atomic Energy

Agency *et al* 2004].

The assessment of treatment planning is performed through the dose-volume histogram (DVH). This tool checks whether the dose delivered to the treatment region aligns with the prescribed dose in the planning phase. The DVH also analyzes the dose deposited in healthy tissues adjacent to the treatment region. The primary limitation of the DVH is that it does not consider radiobiological tissue parameters, considering only the dose deposited in a specific volume [Alva Sánchez and Nicolucci, 2012], [Hernandez *et al* 2020]. This limitation can lead to a reduction in the control of tumor cells, meaning that tumor cells may not be completely eradicated due to the lack of consideration for radiobiological parameters.

The use of mathematical models that include radiobiological parameters allows for considering specific aspects of tumor dynamics. These models are employed to calculate the probability of cells being destroyed based on the deposited dose, known as the probability of tumor control (TCP). TCP can quantify the quality and efficacy of treatment based on cellular radiosensitivity factors [Bloch 2012]. However, relying solely on TCP may not be enough to evaluate radiotherapeutic protocols, as ionizing radiation can damage not only tumor tissues but also healthy tissues, facilitating unwanted effects in regions near the tumor site.

In the late 1980s, the oncology community recognized the importance of analyzing the probability of complications in healthy tissue (NTCP). NTCP quantifies, in probability terms, the complications in healthy tissues adjacent to the tumor region. In a more comprehensive analysis, it is essential to use both NTCP and TCP (tumor control probability) to establish an effective radiotherapeutic protocol that avoids harm from ionizing radiation to healthy tissues [Palma *et al* 2019]. To achieve this, this work aims to identify and evaluate the most commonly used models for TCP and NTCP available in the literature. Relevant studies were selected and analyzed.

Predefined numerical parameters are required to determine the biological response to a radiotherapeutic treatment (TCP and NTCP), such as the cell survival fraction, dose per fraction, clonogenic rates, and the tolerance dose for each tissue. These parameters are typically derived from experimental studies, leading to a significant variability in their values. Therefore, this chapter aims to assess the impact of such parameters on TCP and NTCP models for prostate cancer.

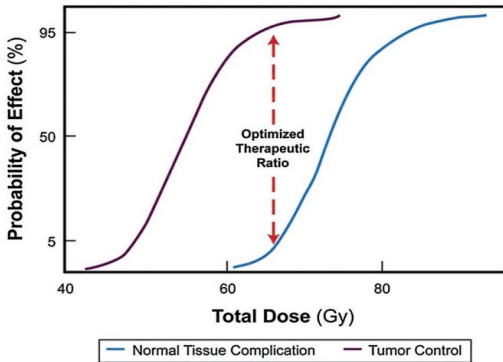
12.2 TCP e NTCP

Tumor Control Probability (TCP) is designed to quantify the success of eradicating tumor tissue. TCP can be used as a criterion to assist in planning, as well as for radiotherapeutic techniques [Alva Sánchez and Nicolucci 2012], [Bloch 2012]. The Normal Tissue Complication Probability (NTCP) assesses the probability of complication in normal (healthy) tissue during radiotherapeutic treatments [Chimin, 2020], [Palma et al 2019]. Both TCP and NTCP demonstrate the radiation dose required to eradicate tumor tissue while minimizing the probability of late complications in healthy tissue.

Figure 1.1 provides a better illustration of the definition and highlights that there is a dose at which the probability of tumor control is much higher than the probability of causing damage to healthy tissue [Bloch, 2012].

Figure 1.1. Schematic curve of TCP and NTCP as a function of dose.

Source: Adapted from [BALAGAMWALA, 2012].



Despite these indicators being an excellent tool in calculating the biological response to radiotherapeutic treatments, the clinical environment usually does not consider radiobiological parameters in dose-response, focusing solely on physical aspects, i.e., only assessing the DVH. The literature provides various mathematical models for TCP [Ballhausen and Belka 2017], [Chimin 2020]. Among them, the Poisson model is the most classic and will be used as a basis in this chapter. In the case of NTCP, the number of models available in the literature is limited, with the Lyman-Kutcher-Berman (LKB) model being the most common.

12.2.1 Modeling TCP: The Poisson Model

The Tumor Control Probability (TCP) aims to quantify the eradication of tumor tissue and, in turn, can be used in clinical settings for plan validation as well as for radiotherapeutic techniques [Alva Sánchez and Nicolucci 2012], [Bloch 2012]. The TCP equation can be described through mathematical models that relate the number of initial cells to the survival fraction of tumor cells, as shown in equation (1) [Bloch 2012]:

$$TCP = e^{N_0 S} \quad (1)$$

where N_0 is the initial number of cells, and S is the cell survival fraction. The cell survival fraction is a relationship that considers the total number of cells before and after tissue irradiation, based on the linear-quadratic model (LQM) [Dawson, 2006], which can be described more intricately, taking into account cell repopulation and addressing important factors that should be considered post-radioinduction of cellular tissue. This model, proposed in 1970, is widely used to quantify the cell survival fraction in tumor tissue and refers to single (α) and double (β) strand DNA breakage. The theoretical fitting of the survival curve allows obtaining an exponential curve given by the equation:

$$S = e^{-\alpha D - \beta D^2} \quad (2)$$

where S is the fraction of cells that survive the total radiation dose D .

To determine the cell survival fraction considering more realistic biological conditions, such as the increase in tumor cells during treatment due to the characteristics of irradiation protocols, a term of cell repopulation is added to the LQM. Thus, a new equation for the cell survival fraction is derived, given by

$$S = e^{[-nd(\alpha + \beta d) + bT]} \quad (3)$$

Where n is the number of fractions, d is the dose per fraction, T is the treatment time, and b is the cellular proliferation rate.

The Poisson distribution describes the Target Theory, which relates DNA damage to a charged particle. Thus, the Poisson model associates the number of hits on targets, i.e., the probability of a particle

not interacting with DNA and, consequently, tumor cells surviving. Poisson statistics are employed in this case due to the extremely small and independent probability of causing damage to a specific region of DNA. Thus, the probability of cell survival, i.e., no DNA break occurring (P_0), can be described by [Chimin 2020]:

$$P_0 = e^{\left(-\frac{D}{D_m}\right)} \quad (4)$$

where D is the total dose, D_m is the dose threshold for target inactivation.

The Linear Quadratic Model (LQM), described based on the Poisson model, analyzes the effect of radiation on a specific biological tissue from the fraction of cell survival, using the parameters α and β to assess the probability of lethal damage through two distinct particles [Ballhausen and Belka 2017], e assim, chega-se a equação (5), que descreve a TCP de Poisson em função dos parâmetros α e β , considerando parâmetros de repopulação celular.

$$TCP = e^{(-S(T_c).e^{\lambda T_c.N_0})} \quad (5)$$

Where λ be the effective rate (cell proliferation rate (b) - rate of cells dying from spontaneous induction (d)), T_c be the time that cells remain non-reproducing, and N_0 be the initial number of cells.

It is important to emphasize that there is a wide range of values for the α and β parameters, which vary according to the aggressiveness of the tumor and its relationship with the use of androgens, hormones commonly used concomitantly with radiotherapy to reduce tumor progression [Mirabell 2012].

This study employed six distinct values to analyze the variation in TCP curves concerning the alpha and beta parameters. The parameters were categorized into low, intermediate, and high tumor risk. The values are presented in the following Table 1.1:

Table 1.1. TCP Parameters for Prostate Cancer

Reference	Level	α (Gy^{-1})	β (Gy^{-2})
Mirabell (2012)	Low	0.010	0.0167
Mirabell (2012)	Intermediate	0.036	0.0212
Mirabell (2012)	High	0.044	0.0275
Pedicini (2013)	Low	0.14	0.044
Pedicini (2013)	Intermediate	0.15	0.048
Pedicini (2013)	High	0.15	0.058
Average	-	0.00883	0.0359

Table 1 illustrates a wide range of values, with a relative standard deviation of approximately 74% for α and 46% for β .

12.2.2 NTCP Modeling: The LKB Model

During the analysis of NTCP, it was observed that predominantly one model, the Lyman-Kutcher-Berman (LKB) model with variations, is widely adopted today [Chimin 2020], [Palma et al 2019]. The LKB model is based on the sigmoid function and the Kutcher-Berman effective volume method. LKB follows a pattern of uniform dose in the organ with a 50% complication risk, indicating that 50% of the cells in the tissue will lose their function (cell death). As mentioned earlier, LKB's NTCP works with a complication of up to 50% of healthy tissue, which can result in various levels of side effects, from the lowest (resection of healthy tissue) to the highest (necrosis of healthy tissue). The equation is expressed by [Chimin 2020]:

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^p e^{-\left(\frac{x^2}{2}\right)} dx \quad (7)$$

Where,

$$p = \frac{D - TD_{50}(v)}{m \cdot TD_{50}(v)}$$

Where D is the dose, v is the fractionated organ volume ($v=V/V_{ref}$), is the reference volume for OAR, m is the organ-specific parameter (represents the dose-response curve gradient), and TD_{50} is the uniform organ tolerance dose with a 50% complication risk. Thus, NTCP can be calculated by the following equation:

$$TD_{50}(v) = \frac{TD_{50}(1)}{v^{nv}} \quad (8)$$

Where, $TD_{50(1)}$ is the total uniform dose that produces a 50% NTCP if the entire organ is irradiated, and nv is the parameter defining the volume dependence on radiation.

The studies on NTCP parameters were conducted through a qualitative analysis. In this context, groups of individuals with the same type of cancer and location (e.g., prostate cancer) were examined to assess side effects in each patient. Based on documented data, ranges of values were established for each parameter.

Due to the nature of the analysis, which is not conducted in vitro, the literature presents a wide range of values for these parameters, making it quite heterogeneous. Given this diversity, articles on NTCP were reviewed, focusing with a particular focus on the years from 2010 onward, to understand how these parameters correlate with LKB TCP (Lyman-Kutcher-Burman model). Table 1.2 provides a specific analysis of some of these parameters for the rectum as the organ at risk, along with their corresponding references.

Table 1.2. NTCP Parameters for Rectum

Reference	n	m	TD ₅₀ (Gy)
Sánchez-Nieto, 2019	0,09	0,13	76,9
Liu, 2010	0,068	0,14	81
Mesbahi, 2019	0,12	0,15	80
Gloi, 2023	0,085	0,27	97,7
Tucker, 2010	0,077	0,146	79,1
Fortes, 2020	0,18	0,16	68,9
King, 2019	0,13	0,15	68,5
Scobioala, 2019	0,06	0,15	80
Zhang, 2022	0,12	0,15	80
Average	0,1033	0,1607	79,122

As illustrated in Table 1.2, parameter value variation is lower than TCP parameters, with a relative standard deviation of approximately 37% for n , 26% for m , and 11% for TD_{50} .

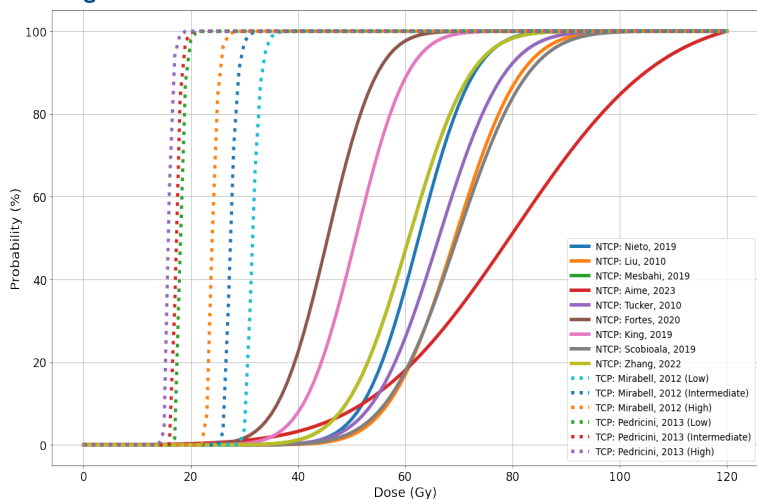
12.3 Analysis of Parameters Applied to TCP and NTCP Models

In this section, the application of the Poisson TCP model and LKB NTCP model will be analyzed, considering a dose range from 1 to 121 Gy to examine the behavior of the curves. For each model, the parameter values from Tables 1.1 and 1.2 were applied. Treatment-related parameters were obtained from the literature or provided by the Centenário Oncology Clinic, located in São Leopoldo, RS, Brazil. Figure 1.2 presents the obtained results.

Table 12.3. Values of the treatment parameters used for curve construction

Parameter	Value	Reference
T	52 days	Protocol of Centenário Oncology Clinic
T_c	28 days	Bloch (2012)
T_d	42 days	J.Z. Wang et al. 2005
N_0	10^7 cells	J.Z. Wang et al. 2005
d	2 Gy	Protocol of Centenário Oncology Clinic
n	37 fractions	Protocol of Centenário Oncology Clinic

Figure 1.2. Curves of Poisson TCP and LKB NTCP as a function of dose



When analyzing the graph, it is observed that the TCP curves from the Pedricini (2013) reference indicate a tumor control of 100% from a total treatment dose of 18 Gy, with minimal dose variation. On the other hand, the Mirabell reference (2012) TCP curve achieves 100% tumor control from

22 Gy, varying up to about 30 Gy. It is worth noting that curves further to the left indicate better treatment outcomes, i.e., a smaller amount of dose is required to eradicate around 100% of the tumor volume.

Regarding the rectal NTCP, for the same evaluation criteria, the complication risk reaches 50% from a total treatment dose of 42 Gy in the Fortes (2020) reference. In the Scobioala study (2019), the same effect is observed but only from a total dose of 70 Gy. Considering the dose range used in prostate cancer treatments, which varies between 60 Gy and 74 Gy, it is observed that the risk of complications in healthy tissue remains low, especially when considering the parameters provided by the Scobioala study. This conclusion is reinforced by the clinical study analysis, revealing that approximately 50% of the organ volume in question receives around 50 Gy. Thus, despite the discrepancy, there is an "optimal" range of variation between high TCP and low NTCP, between 30 Gy and 42 Gy.

12.4 Conclusion

It is observed that changes in parameters, both in TCP and NTCP, impact the analysis of tumor dynamics. This scenario motivates the search for parameters that result in an "optimal" range of variation between TCP and NTCP, preferably aligned with clinical practice. Conducting further studies on analyzing these parameters is necessary to establish a threshold considered optimal.

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13 Improving the Pharmaceutical Care Experience through the Integration of New Technologies: The Case of Telepharmacy

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Abstract:

This chapter describes Pharmaceutical Care improvements through the integration of telepharmacy technology. We found evidence that despite the limitations (i.e. need for infrastructure, implementation and maintenance costs); telepharmacy has the potential to positively impact the patient experience with more expanded and convenient primary care services. Further studies are needed to bring evidence about patient experience improvements in primary care.

Keywords: Pharmaceutical Care; Primary Health Care; Telepharmacy; Pharmacist; Pharmaceutical Services.

Sustainable Development Goals (SDG): Good health and well-being; Quality Education; Reduced inequalities.

13.1 Introduction

Pharmaceutical care is an approach that guides the provision of pharmaceutical services based on the humanisation of health care, aiming at health prevention and overcoming barriers to treatment adherence. In this context, the pharmacist plays an important role in providing support to patients during the treatment process, which covers both the pharmacological and non-pharmacological aspects of disease management, especially in the case of chronic diseases (Cipolle et al., 2012; Hepler & Strand, 1990). Integrating technologies in this context can benefit patients who can receive assistance more widely and conveniently (Omboni & Tenti, 2019). Telepharmacy studies and implementation initiatives have recently become more relevant for health managers as they have the potential to overcome barriers to pharmaceutical care implementation (Baldoni et al., 2019; Omboni & Tenti, 2019). In this context, the patient perspective can provide insights into planning and improvement of service and achieve better standards of quality (Litovuo et al., 2018; National Health Service Institute, 2013). In this chapter, we will discuss how the integration of pharmaceutical care, telepharmacy and patient experience studies can benefit patients and the provision of healthcare services.

13.2 Pharmaceutical Care

Pharmaceutical care is an approach that guides the provision of integrated pharmaceutical services into the health system network focused on patient needs (American College of Clinical Pharmacy, 2008; Conselho Federal de Farmácia, 2016). Pharmaceutical services is a concept that includes any activity in healthcare which has medicines as an essential item for care provision, and the pharmacist is the health professional responsible for its coordination (American College of Clinical Pharmacy, 2008; Conselho Federal de Farmácia, 2016). Clinical pharmaceutical services are a part of it, characterized by a set of activities provided directly by the pharmacist, including but not limited to services such as preparing discharge prescriptions, medication review, pharmacotherapeutic monitoring, screening tests, and disease management. Pharmaceutical care is the logic that organizes these pharmaceutical services to meet the patients' needs for disease prevention, promotion, diagnosis, protection, and health recovery (Conselho Federal de Farmácia, 2016; NHS England, 2019).

The results found in the literature are optimistic regarding the effect of pharmaceutical care on population health. researchers in the area have demonstrated that it positively influences the management of chronic health problems, such as diabetes, hypertension and asthma (Pande et al., 2013; Yuan et al., 2019). Also, health managers and researchers worldwide suggest that harnessing pharmacists' skills through the implementation of pharmaceutical care is a feasible pathway to optimizing human resources in the healthcare system, improving patients' quality of life and reducing health inequalities, although more evidence is still needed (NHS England, 2019; Pande et al., 2013; Thomson et al., 2019).

Due to its public health potential, health managers have encouraged the implementation of pharmaceutical care in health services, including community pharmacies and primary healthcare units (Brazil, 2015; NHS England, 2019; Rigo et al., 2023). Nevertheless, the effective implementation of Pharmaceutical Care has encountered cultural, technical, political and managerial challenges (Brazil, 2022; Rosenthal et al., 2016). This approach represents a slow cultural shift unfolding over the past two decades, a relatively recent period compared to the history of the pharmacist profession. This shift redirects the care focus from the medicine product to care centered on the patient's needs (Cipolle et al., 2012; Rosenthal & Holmes, 2018; Vieira, 2007). Therefore, great efforts have been made and are still needed to show evidence, advocating for the advantages of this approach, training pharmacists, and reorganizing pharmacies and other health services strategically for the Pharmaceutical Care practice (Brazil, 2022).

13.3 The Patient Experience

Patient Experience in healthcare can be defined as "how the patient feels during the process of receiving care" (National Health Service Institute, 2013). The experience is a subjective aspect; however, it could be objectively related to the patient's clinical outcomes and, ultimately, can influence their adherence to health services and prescribed treatment (Doyle et al., 2013; Hanefeld et al., 2017).

This study has aroused the interest of health researchers and managers because it can provide valuable information to improve healthcare services (Berry & Bendapudi, 2007; Doyle et al., 2013; Lima, 2020). Analyzing the patient perspective is essential for enhancing quality and patient-centeredness and guiding the successful implementation of

health services (Beleffi et al., 2021). Designing or redesigning services based on patient experience studies helps to provide a better experience for individuals seeking the “provision of a service that is required, but not always desired”, thereby promoting adherence to the treatment and the health service and, consequently, improving clinical and economic outcomes (Doyle et al., 2013; Lima, 2020; Litovuo et al., 2018).

Furthermore, patient experience studies help assess health service quality and support telehealth implementation. Accessibility, acceptability, and equity are three of the quality features in health services that exploratory research in patient experience can help to provide insights into the matter, and those features are particularly relevant for telehealth interventions (Eze et al., 2020; Lindkvist et al., 2021; Wang et al., 2021). This is because patient experience studies can identify opportunities to improve flows and optimize the use of information and communication technologies in favor of the patient, strengthening humanized, practical, and sustainable health services (Oehrlein et al., 2023; Stroetmann et al., 2010).

13.4 The Telepharmacy

Telepharmacy can be defined as Pharmaceutical Care in which pharmacists and patients are not in the same place and can interact through Information and Communication Technology (ICT) resources (Baldoni et al., 2019). This service proposal was primarily designed to serve patients remotely to expand healthcare access and improve patient safety and therapeutic results (Omboni & Tenti, 2019). Additionally, telepharmacy allows the delivery of pharmaceutical services in scenarios with a shortage of human resources, presenting as an alternative to minimize this problem, especially in remote regions (Baldoni et al., 2019).

Following this, different countries have been driving efforts to implement telepharmacy services, such as the United States, Spain, Denmark, Egypt, France, Canada, Italy, Scotland, and Germany (Baldoni et al., 2019). Recently, in Brazil, telepharmacy has been formally regulated, breaking down into different concepts according to their finality: pharmacist teleconsultations, tele-inter consultations, telemonitoring/telesurveillance and teleconsulting (Conselho Federal de Farmácia, 2022). These initiatives are related to the evidence that the literature has been showing, such as helping health managers in service planning (Gossenheimer et al., 2021), promoting patient adherence to treatment among polypharmacy elderly

(Rebello et al., 2017), improving patient safety in antineoplastic medicine preparation (Gordon et al., 2012), providing health education for patients with asthma and chronic obstructive pulmonary disease (Brown et al., 2017; Margolis et al., 2013), and making teleconsultations to identify medication-related issues feasible in remote areas (Amkreutz et al., 2020).

After 2020, the slow implementation of telehealth strategies in health systems worldwide suddenly experienced rapid growth due to the COVID-19 pandemic prevention measures and more studies on telehealth were published (Organization, 2021). In this same context, more evidence of telepharmacy became available (Dat et al., 2023). This was due to the increasing offer of telepharmacy services, as remote dispensing and counseling proved to be effective measures to avoid infection (Dat et al., 2023). A systematic review of field application, benefits, limitations, and applicability in the COVID-19 pandemic identified 39 articles and suggested that telepharmacy played an essential role in addressing pharmacist shortages and helping patients both safely and effectively administer medications in underserved areas (Dat et al., 2023). The promising results were limited to the COVID-19 pandemic; therefore, more studies are needed to verify the same features in other contexts.

Despite the growing literature on the evidence of telepharmacy benefits after the COVID-19 pandemic, there are still gaps in understanding the impacts of this service. Regarding the clinical effectiveness of telepharmacy diabetes services, a systematic review and meta-analysis associated it with a decrease in HbA1c levels (Difference in the Mean – 1.26%; 95% CI –1.69 to –0.84) from baseline and lower risk of hypoglycemia (Relative Risk 0.48; 95% CI 0.30 to 0.76) when compared to non-telepharmacy service (Cao et al., 2022). However, regarding the effect of telepharmacy services in the community pharmacy setting on quality of care and patient safety, a systematic review identified 866 studies, of which only six met the inclusion and the risk of bias measurement criteria; those studies evaluated the outcomes of patient satisfaction (n=3), medication dispensing errors (n=2), adherence (n=2), and inappropriate use (n=1) (Pathak et al., 2021). A scoping review identified 52 articles regarding medication adherence improvement and suggested that telepharmacy can improve medication adherence in older people (Emadi et al., 2022). Moreover, the study found that service-related factors (design, commercial aspects, adherence measurement, and communication with the health care team), along with patient-related factors (health constraints behaviors,

digital skills training, and perceptions), can impact the effectiveness and efficiency of this service (Emadi et al., 2022).

Thereby, telepharmacy has the potential to broaden the availability of a different range of pharmaceutical services, positively influencing the patient experience with health services (Le et al., 2020; Viegas et al., 2022). Implementation studies of telepharmacy that measure patient satisfaction often show a medium-high level of satisfaction among patients (Baldoni et al., 2019). However, it is noteworthy that patient experience studies are not limited to measuring patient satisfaction levels (Hanefeld et al., 2017). Patient Experience is a broader study area, qualitative by nature, of how patients feel interacting with the health service (Hanefeld et al., 2017; Litovuo et al., 2018). Patient experience studies in tele pharmaceutical care services could offer a unique opportunity to identify how and when patients want to interact with health services through ICT, making it feasible and appropriate to the reality of this public (Forésti & Oliveira, 2021; McCarthy et al., 2016).

13.5 Final considerations

Implementing pharmaceutical care services in the healthcare system can improve public health outcomes (Pande et al., 2013; Yuan et al., 2019). Reducing premature mortality caused by chronic non-communicable diseases and access to quality essential health services is one of the Health and Well-being objectives of the United Nations Sustainable Development Goals (SDGs) that Pharmaceutical Care can help to achieve (Nações Unidas, 2023; Pande et al., 2013; Yuan et al., 2019). Furthermore, using information and communication technologies to mediate pharmaceutical care is a promising pathway to overcome implementation barriers and increase pharmaceutical services availability (Baldoni et al., 2019; Le et al., 2020; Viegas et al., 2022). However, more studies are needed to show evidence of the contribution of telepharmaceutical services to public health.

Future studies on patient experience in the context of pharmaceutical care may be fundamental to implementing in-person and remote sustainable and humanized pharmaceutical services (Brazil, 2022; Rosenthal et al., 2016; Soeiro et al., 2017). We believe that future investigations exploring the intersection between the concepts of pharmaceutical care, patient experience and information and communication technologies can provide the practical and theoretical basis to fill this gap and consolidate the pharmaceutical care practice in the

healthcare system.

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14 Mapping and Application of Lean Healthcare in Electrotherapy in a Hospital Physiotherapy Service

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Abstract:

Tertiary-level healthcare services exhibit significant complexity in their physical-functional structures and the diverse range of specialized resources needed for operation, leading to substantial costs. This poses a challenge for efficient management aiming at sustainability. Whole-body electrical stimulation in hospital settings offers various therapeutic benefits that improve clinical outcomes and enhance patient care. In this context, the Lean methodology is based on continuous quality improvement, aiming to reduce waste and displaying flexibility in its application. This research aims to map and apply the lean methodology in the electrotherapy process in a national reference hospital complex. It is an exploratory case study that utilizes the Lean approach to design the process and its value stream mapping tool to list opportunities for improvement.

Keywords: Lean healthcare; Physiotherapy; Electrical Stimulation, Health Management.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

14.1 Introduction

Tertiary health services involve complex physical-functional structures and a wide range of specialized human and material resources necessary for their operation. This requires significant financial investments for ongoing technical and scientific updates, posing challenges to sustainability. Thus, the management of the service becomes a challenge for hospital institutions. In the context of healthcare, the performance and qualification of the multi-professional team have a significant impact on patient care in various aspects: safety and quality, management of surgical patients, oncology and palliative care patients, critically ill patients, education and health promotion, among others, adding value to the patient experience and improving patient performance in the hospital environment. In this scenario, technological innovations align with this qualification and value in health, specifically, in this work, the use of whole-body electrical stimulation by the physiotherapist.

Electrical stimulation can be used for various purposes such as analgesia, recovery of motor strength, mobility, treatment of pressure ulcers, urinary incontinence, constipation, and nausea, among others, reducing the use of medications, and in some cases, the length of hospitalization. Balancing healthcare quality, advanced technology use, specialized labor, and limited resources presents a significant challenge for managers aiming for system sustainability. The fragility of this system, coupled with the demand for more efficient management, supports the adoption of methods and tools typically used in manufacturing, adapted specifically for the healthcare sector, with an emphasis on Lean Production.

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When applied to healthcare services, it improves performance and increases organizational competitiveness. Literature indicates an increasing trend in applying lean healthcare methodologies to healthcare services. The emergency sector is often highlighted due to its inefficiencies and the consistent demand that makes it suitable for process improvement applications. Bem-Tovim (2008), in his study, describes the implementation of Lean healthcare in the emergency department of a hospital in Australia in three stages: acquiring technical knowledge, stabilizing high volumes of service, and normalizing and sustaining changes. The result was a doubling

of daily service in the sector with a reduction in the number of patients who give up on treatment due to service delays. In Brazil, Netto demonstrates improvement actions proposed by the Lean methodology in the patient registration process at a physiotherapy center in Rio de Janeiro. Through tools such as value stream mapping, 5W2H, Pareto chart, and A3 report, measures were identified and adopted to optimize the registration process. This included reducing unnecessary professional travel, reorganizing professional functions, and implementing electronic health records to minimize repetitive document searches. This resulted in process optimization and an expected improvement of 35% in Lead Time and 80% in opportunity time. Additionally, the reallocation of time is equivalent to 24 physiotherapy sessions, allowing an inference of an increase in the unit's service capacity.

This study is relevant as mapping the current electrotherapy process enables the identification and visualization of improvement opportunities through the application of Lean methodology, leading to a proposed future flow mapping. This mapping will be validated by experts using the Delphi method. The future proposal aims to eliminate unnecessary steps, optimize service delivery, expand patient reach, and add value to positive outcomes. Additionally, resource allocation will be optimized, potentially reducing costs for healthcare services. Therefore, this study seeks to map and analyze the use of electrical stimulation within a national reference hospital complex and apply Lean methodology to future flow mapping and identify opportunities for improvement.

The use of electrical therapy for medical purposes dates back to ancient times. The Abyssinians, who inhabited present-day Ethiopia, were among the first to use this method, employing electric fish for treatment. Although there are no written records, depictions on the walls of Egyptian pharaohs' tombs from the Fifth Dynasty (circa 2740 B.C.) suggest its application. Around 36 A.D., during the reign of the Roman Emperor Tiberius, Anthero, a freed slave, experienced foot pain caused by gout. While walking along the beach, he encountered an electric fish, and after being shocked, his pain subsided. Scribonius Largus (46 A.D.), the emperor's physician, upon learning of this, advocated for using electric fish to treat neuralgia, arthritis, and headaches, noting that the paresthesia was gradual and persisted after contact ended. In 1791, Luigi Galvani, while conducting experiments, accidentally discovered that the muscles of a dead frog contracted when exposed to electrical stimulation. His nephew, Giovanni

Aldini, later applied these stimuli to the cadavers of recently executed criminals. Studies in this field continued, and following the IX International Congress of the World Confederation for Physical Therapy in 1982 in Stockholm, electrotherapy was introduced in Brazil, spurred by a request from a national equipment manufacturer for electroanalgesia, the TENSYS 831.

Electrical stimulation has resurged in modern times due to two important factors: technological advances and neurophysiological discoveries in pain and analgesia mechanisms. It is defined as the use of electric current modified by therapeutic equipment. Physiotherapy professionals use this method to treat various health conditions in both intra and extra-hospital environments. When establishing therapy for muscle contraction, it is essential to highlight the difference between contraction caused by voluntary activation and electrical stimulation. In the former, motor recruitment is synchronous, while in the latter, it is asynchronous.

Furthermore, electrical stimulation can induce local metabolic changes compared to voluntary contraction, supporting the technique's applicability as an adjunct in cases of muscle atrophy. There are also effects on microcirculation through the mobilization of endothelial progenitor cells through electrical stimulation. These cells play a role in neovascularization, repair, and endothelial restoration, allowing for the benefit of therapy in the recovery and treatment of pressure ulcers(3).

Centuries ago, electrical stimulation therapy was already used for analgesia, with its use enhanced by technological advances. Studies indicate benefits in preventing critical patient polyneuromyopathy and reducing mechanical ventilation time when electrical stimulation is applied to critical patients' lateral, medial, and fibular muscles. When associated with an exercise protocol, it reduces sedation time positively. However, when associated with an early mobilization protocol, whole-body vibration platform, or cycle ergometers, there is no improvement in results. Nevertheless, it has the limitation of discomfort associated with peripheral stimulation through electrical stimulation.

The history of Lean production dates back to the 19th century when Sakichi Toyoda, founder of the Toyota Group in Japan, invented a loom that would stop functioning if any of its threads broke. This was a revolutionary idea at the time, as it enabled the automation of looms, allowing a single operator to control multiple machines simultaneously. Thus, Toyoda

increased production and saved money by halting the process when a fabric defect occurred. This introduced the principle of performance improvement, where the process is interrupted in case of a defect, eliminating time loss, reducing the number of defective products, and maintaining continuous flow. (4,5)

The shift in the production system, eliminating waste and continuous improvement associated with worker development and reasoning, led Toyota's executive leadership to refer to the Toyota Production System as the "Thinking People System". (5,6) The system's flexibility and ability to adapt to changes and its emphasis on promoting continuous quality improvement by reducing waste through strategic thinking, facilitated its expansion beyond industrial applications to include the healthcare sector.

The introduction of Lean thinking in healthcare, or Lean Healthcare, was catalyzed in 2006 when the Lean Enterprise Academy (LEA) in Britain organized the first congress on the applicability of Lean in healthcare services. It is based on two key elements: value and the pursuit of excellence through the elimination of waste/loss. (7) Value, value chain, continuous flow, pull production, and perfection constitute the principles of the Lean philosophy.

Value is created by reducing waste. When applied to service delivery, it is crucial to consider the offered product's value and, from the customer's perspective, what its value is. This thinking then continues into the value chain. The value chain consists of a set of activities necessary to generate the product, from production to its arrival at the end customer. Determining what adds or does not add value in these stages is the next step in Lean thinking. Liker (2005) suggests that, when discussing activities, they can be classified into three groups (8):

- a) Value-adding activities: making the product valuable, allowing customers to spend more to obtain it.
- b) Non-value-adding activities: irrelevant during production and should, therefore, be excluded.
- c) Non-value-adding, but necessary activities: actions that do not add value to the end customer but are important in the production chain.

Thus, it is possible to list wastes to eliminate them, optimize the production process, and generate value for the final product or service offered (9).

In continuous flow, it is possible to visualize the production process smoothly after eliminating waste or errors, aiming for the shortest

processing time and lower cost (10). Furthermore, it refers to the inherent processes for the final product, allowing minimization of inventory formation or excessive steps for the flow of information and product.

Pull production depicts production according to demand. In other words, products are replenished or produced according to their consumption by customers. Perfection is under the perspective of continuous improvement of activities due to the possibility of faults that may interfere and invalidate or compromise the entire production process. Continuous improvement and perfection go hand in hand in Lean within a company, as the value chain must be constantly reviewed to understand customer needs and expectations and reduce waste (11).

The seven wastes/losses in healthcare are transport, inventory, waiting, overproduction, defects, excessive movement, and inappropriate processing, exemplified in the table below.

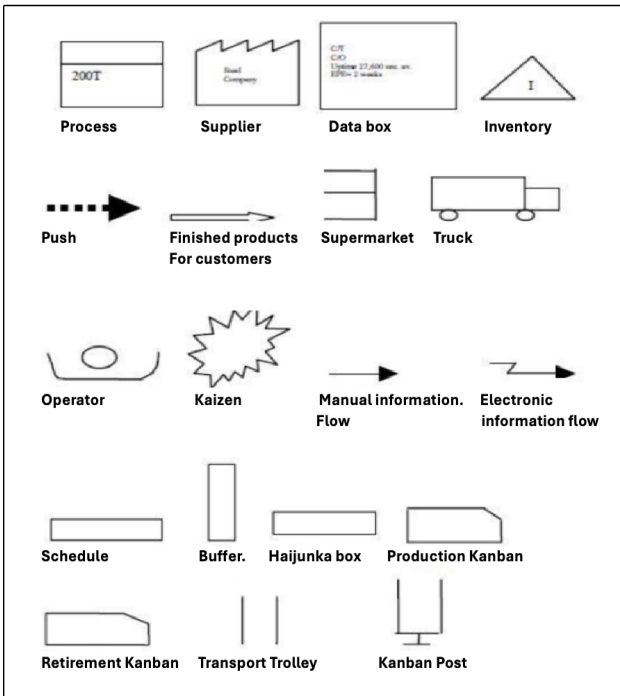
Table 1.1. Types of Waste in the Hospital.

Waste Category	Manufacturing	Healthcare
Overproduction	Producing too much or too early, resulting in excess inventory.	Documentation, redundant processes, redundant tests, unnecessary procedures.
Defects	Frequent errors in information processing, product quality issues, or low delivery performance.	Performing tests inappropriately, medication or diagnostic errors.
Unnecessary Inventory	Excessive storage or waiting for necessary information or products, resulting in excessive cost and low customer service levels.	Waiting for expected lab results or even patients waiting for diagnoses can be considered inventory.
Inappropriate Processing	Executing the process with tools, procedures, or systems that are not suitable, to the detriment of simpler and more efficient approaches.	Unnecessary tests, the use of broad-spectrum antibiotics for the treatment of mild inflammations.
Excessive Transportation	Excessive transport of goods or information, resulting in increased time, effort, and cost.	Transporting medications, patients, laboratory tests.
Excessive Movement	Excessive movement of people, moving and storing parts, including unnecessary physical movements of operators.	Excessive movement of the healthcare team due to poorly planned layouts.
Waiting	Long periods of inactivity of people, information, or goods, result in poor flows and long lead times.	The time during which the patient waits for a bed, waits for the results of a test, for their treatment, or for hospital discharge.

Source: Adapted from Guimarães (2018) and Souza (2020).

Among the tools used for Lean implementation, Value Stream Mapping (VSM) was employed. This involves mapping the entire process and illustrating the flow of materials, people, and information involved. VSM is a tool that helps visualize weaknesses, delays, and bottlenecks in the process, facilitating the identification of improvement opportunities. It provides detailed visibility of the various stages within the process and supports managers in decision-making. VSM can be utilized for mapping current processes as well as depicting a future state. Creating a VSM requires the use of symbols that represent different aspects of the process, such as physical elements, workflows, information, or orders, among others, as shown in the figure adapted from Rothes and Shook (2003).

Figure 1.1. Identifier Symbols for the Process

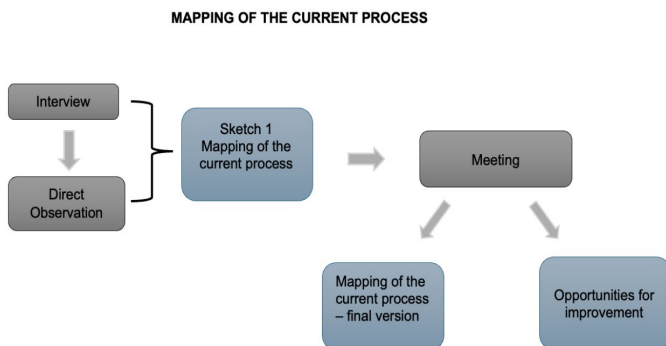


Lean production focuses on eliminating waste. Waste is defined as the consumption of resources that do not generate cost savings or add value to the product. Additionally, lean production comprises a set of principles and techniques. The principles align with the company's philosophy and form the foundation for guiding strategic lean actions. The techniques represent the methods through which these principles are implemented and sustained. Key principles include determining customer value, defining the value stream, maintaining continuous flow, integrating the supply chain, prioritizing quality, utilizing technology that supports employees and processes, and fostering human resource development and continuous improvement. Notable techniques include value stream mapping (VSM), just-in-time, kanban, 5S, standardization, workload leveling, group technology, zero-defect quality control, total productive maintenance, and teamwork.

14.2 Methodology

This study is a case study, defined as investigative research into current phenomena within their real-world context, particularly when the boundaries between the phenomenon and the context are not clearly delineated. The focus of this study was on the processes involving the use of electrical stimulation by the Hospital Physiotherapy Service of a Hospital Complex. The process mapping was conducted in two stages: current process mapping (Figure 1.2) and future process mapping (Figure 1.3), which included identifying improvement opportunities. The current process mapping was performed entirely in person. The validation of the future process mapping is ongoing and is being conducted virtually due to some experts being located outside Porto Alegre. The research involved professionals who had been working in the Hospital Complex for at least six months for the current mapping phase. For the future mapping phase, the study included physiotherapy experts with at least two years of experience in electrical stimulation, health management professionals, or engineers with at least two years of professional experience and expertise in Lean healthcare.

Figure 1.2. Mapping of the Current Process



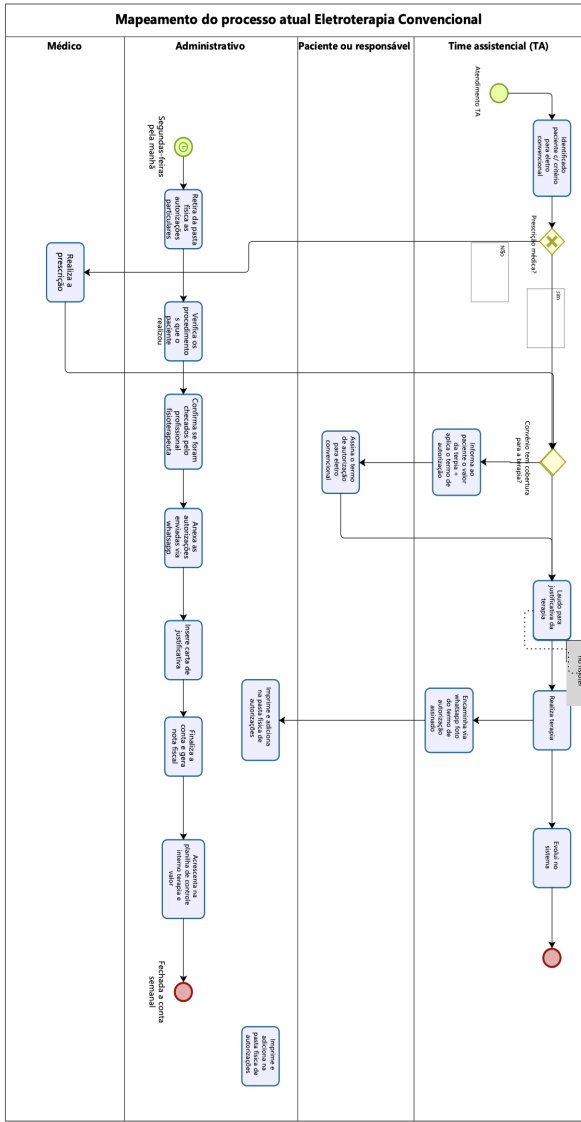
For the mapping of the current process, an interview was conducted with an administrative professional, the physiotherapy leadership responsible for the whole-body electrical stimulation team, a physiotherapist applying conventional electrical stimulation, and two physiotherapists responsible for applying whole-body electrical stimulation. It took around 20 minutes and covered questions related to therapy requests, professionals making requests, where they make them, authorization requirements, eligibility criteria, and the process for closing the account, including coverage by insurance and therapy duration.

Direct observation had no intervention from the researcher and involved three direct observations on different days and times of the week to check for interference related to the shift or time. Combined with the interview, direct observation allowed the creation of the initial draft of the current process mapping to be presented to the participating team, including the physiotherapy manager and the Quality and Patient Safety professional. The purpose was to present professionals with the initial sketch of the mapping and discuss it. This mapping stage took about 1 hour.

14.3 Results and Discussion

Regarding direct observations, it was not possible to follow the professional applying conventional electrical therapy due to its punctuality in request and application, for example, for nausea improvement or localized pain. Therefore, for the elaboration of this mapping (Figure 1.4), interviews and discussions conducted in the meeting stage were used.

Figure 1.4. Mapping of the Current Process of Conventional Electrical Stimulation



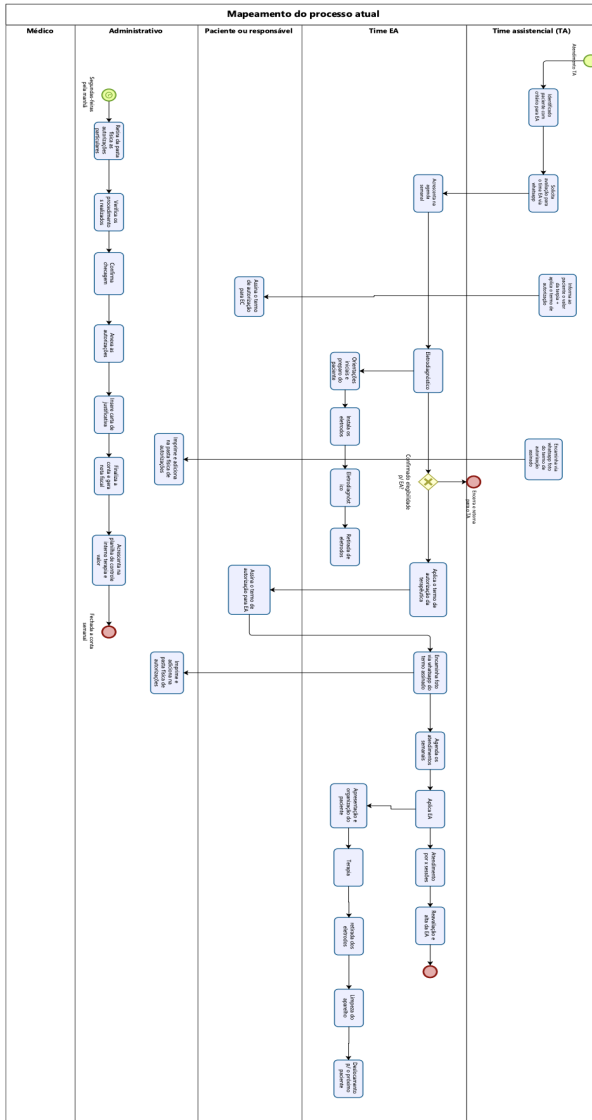
Observations of the administrative professional confirmed a weekly routine, on a set day and shift, for account closure.

The step-by-step process, whether it is whole-body or conventional electrical stimulation, and the disparities between them, especially the fact that whole-body electrical stimulation is private or provided free of charge to public insurance patients. Meanwhile, conventional stimulation can be free, private, or covered by insurance. This affects the authorization dynamics and time for therapy application and, consequently, completion of therapy.

When accompanying physiotherapy professionals applying whole-body electrical stimulation, differences can be observed regarding the first visit related to electrodiagnosis to confirm the patient's eligibility for therapy and the subsequent days when the treatment has already started (Figure 1.5). Patient management occurs weekly, with daily adjustments to the service schedule due to spontaneous demands or patient unavailability caused by tests, clinical issues, or concurrent appointments with other professionals.

Also, it was not clear to the observer the number of sessions for therapy discharge per patient, although there is no doubt about the therapy's benefit to the patient. Additionally, there are significant opportunities to enhance weekly schedule management and inter-team communication.

Figure 1.5. Mapping of the Current Process of Whole-Body Electrical Stimulation.



The listed improvement opportunities have a positive impact on process quality. Prioritizing tasks in weekly management reduces the time spent by professionals. Additionally, implementing visual management and ensuring predictability in therapy discharge will enable physiotherapists to spend less time adjusting schedules or visiting units without providing effective care, resulting in an expected 33% reduction in lead time.

A comparable 35% reduction in lead time was observed in Netto's study, which applied Lean methodology to the patient registration process at a physiotherapy center in Rio de Janeiro. Measures included reducing unnecessary staff movement, reorganizing professional roles, and digitizing medical records. (10) Ben-Tovim (2008) supports these findings, illustrating the benefits of Lean methodology implementation in an Australian hospital's emergency department. The approach was executed in three stages: acquiring technical knowledge, stabilizing high service volumes, and standardizing and sustaining changes. This resulted in doubling the number of daily appointments and a reduction in patients abandoning care due to delays. (12)

The mapping of the future process with improvement opportunities is currently underway. It is recommended that, once the instrument and actions are validated, the PDCA cycle be utilized for planning, development, evaluation, and corrective actions during implementation. Additionally, as this is an emerging innovation and the initial flowchart is being developed, it should be reviewed after one year. Since the study began, the product has matured, the team has grown, and the goal of continuous improvement has been maintained.

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15 An Algorithm for Achieving the Spread-Out Electron Peak in the Focused VHEE Radiotherapy

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Abstract:

Recent studies have shown that depth-dose curves obtained from very high-energy electron (VHEE) radiotherapy can be modulated by controlling the electron beam focusing. In the focused VHEE radiotherapy, by combining beams with different focal points, it is possible to generate a plateau of maximum dose deposition called the spread-out electron peak, analogous to the spread-out Bragg peak in proton therapy. However, achieving the spread-out electron peak is challenging, due to the many degrees of freedom involved. This work proposes an optimization algorithm for obtaining the spread-out electron peak in focused VHEE radiotherapy. In a set of 15 Monte Carlo simulations, the focal position of an electron beam with an average energy of 250 MeV was varied along different depths of a $30 \times 30 \times 30$ cm³ water phantom irradiated by this beam. Once the user defines the region of interest for generating the spread-out electron peak, the proposed algorithm selects the appropriate depth-dose curves and performs a weighted sum of them, optimizing the weighting coefficients that minimize an objective function that relates the standard deviation and the mean dose at the spread-out electron peak. Thus, the algorithm provides the best plateau that can be obtained from the available curves.

Keywords: VHEE; Monte Carlo; Optimization algorithm; SOEP.

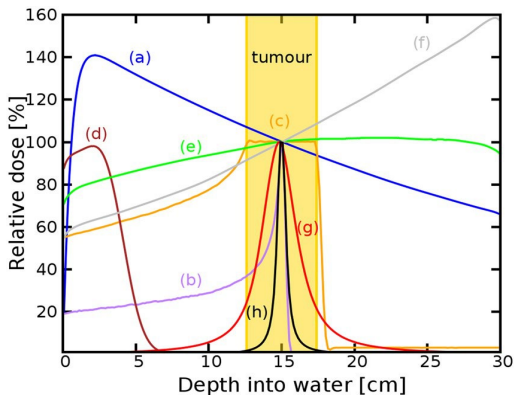
Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

15.1 Introduction

Despite very-high-energy electron (VHEE) therapy being proposed over two decades ago [Papiez et al. 2002] [DesRosiers et al. 2000], the unavailability of clinical accelerators capable of producing beams with the required energies has resulted in limited progress in the study of this therapeutic modality. The development of laser-driven plasma accelerators, capable of generating acceleration gradients on the order of GeV/cm [Esarey et al. 2009] [Kurz et al. 2021], may pave the way for the development of compact and cost-effective accelerators for VHEE radiotherapy applications. Compared to proton therapy, VHEE therapy exhibits a depth dose distribution characterized by high dose deposition both at the entry and exit points of the patient. However, recent computational and experimental research [Kokurewicz et al. 2019] [Kokurewicz et al. 2021] [Brunetti 2021] [Whitmore et al. 2021] [Liu et al. 2023] [Krim et al. 2023] suggests that it is possible to modulate the depth dose distribution in VHEE therapy by controlling the electron beam focusing. Figure 1 illustrates a comparison of depth dose distributions produced by photon beams, proton beams, conventional electron beams, collimated VHEEs, and focused VHEEs. Furthermore, by combining beams with different foci, it is possible to create a depth dose profile with a plateau of maximum dose deposition, referred to as the spread-out electron peak (SOEP), similar to the spread-out Bragg peak (SOBP) achieved in proton therapy, with low dose deposition before and after this plateau.

With the integration of novel electron acceleration technologies and sophisticated dose modulation strategies through beam focusing, focused VHEE therapy has the potential to emerge as a compact and cost-effective alternative to proton therapy. By leveraging dosimetric properties comparable to proton therapy, focused VHEE therapy offers a promising solution for specific treatment sites. Additionally, the potential for lower costs arises from the possibility of mastering and scaling up the required technologies. However, achieving the desired SOEP through the combination of multiple percentage dose-depth (PDD) curves generated with varying electron beam focuses remains a non-trivial challenge. This complexity stems from the numerous degrees of freedom involved, including the number of curves and focuses required, irradiation times for each focus, and optimization of dose distribution.

Figure 1. PDDs of different types of radiation in a water phantom [Kokurewicz et al., 2021]. (a) 6 MV photons, (b) 147 MeV proton Bragg peak, (c) SOBP (Spread-Out Bragg Peak), (d) 10 MeV electrons, (e) 200 MeV collimated electrons, (f) 2 GeV collimated electrons, (g) 200 MeV electrons focused at 15 cm, (h) 2 GeV electrons focused at 15 cm.



This study presents an algorithm that optimizes a SOEP by selecting and weighting pre-calculated focused PDDs based on a defined region of interest (ROI). The algorithm utilizes 15 pre-computed Monte Carlo simulations of a 250 MeV electron beam focused at different depths within a water phantom. By minimizing the coefficient of variation of dose within the ROI, the algorithm determines the optimal weights for each PDD. This yields a weighted sum representing the relative proportions (or irradiation times) of each focused beam needed to achieve the desired SOEP profile. The proposed algorithm can be integrated into future focused VHEE therapy equipment software, providing automated information for achieving planned dose profiles.

15.2 Methods

15.2.1 Monte Carlo Simulations

Monte Carlo (MC) simulations were conducted using the TOPAS (Tool for Particle Simulation) code [Perl et al. 2012] [Faddegon et al. 2020]. The beam was defined with 10^8 electrons, featuring Gaussian distributions in space (with $\sigma_x = \sigma_y = 4$ mm) and in energy ($E_k = 250$ MeV and $\sigma_{E_k} = 0.75$ MeV). The target object is a cubic phantom with dimensions $30 \times 30 \times 30$ cm³ filled with water, and the simulation world was filled with air. The

deposited dose in the phantom was obtained using a DoseToMedium volume scorer that voxelized the phantom into $100 \times 101 \times 101$ bins in the z, x, and y coordinates, respectively. The standard deviations of the deposited dose in each voxel were also computed, with all data being recorded in comma-separated values (CSV) format.

The geometric configurations and parameters adopted in the simulations are based on the study by Whitmore [Whitmore et al. 2021], which, to achieve beam focusing, adopted a system of four sequential magnetic quadrupoles, q_1 , q_2 , q_3 , and q_4 , separated by distances $d_1 = 109$ cm, $d_2 = 206.9$ cm, $d_3 = 237.8$ cm, $d_4 = 416.1$ cm, and $d_5 = 462.2$ cm. The quadrupoles were incorporated into TOPAS using the component QuadrupoleMagnet, with two of them being defocusing (q_1 and q_3) and two focusing (q_2 and q_4). All quadrupoles have the same dimensions of $40 \times 40 \times 18$ cm³. The beam propagates in the direction of the z-axis, passing through the center of the quadrupoles and impinging on the phantom. The physical modules used in TOPAS originate from the Geant4 code, namely, g4em-standard_opt4, g4h-phy_QGSP_BIC_HP, g4ion-binarycascade g4decay, g4h-elastic_hp, and g4stopping.

In the simulations, varying the magnetic field gradient of the last quadrupole, denoted as g_4 (as detailed in Table 1), enabled the generation of distinct focal positions distributed throughout the depth of the phantom. The gradients of the remaining quadrupoles, namely q_1 , q_2 , and q_3 , remained constant at $g_1 = 10.5$ T/m, $g_2 = 10.6$ T/m, and $g_3 = 8.0$ T/m, respectively.

Table 1. Values of g_4 , the gradient of the magnetic field in the quadrupole q_4 , and the respective positions of the PDD peaks in the phantom, corresponding to the focal positions of the electron beam obtained from TOPAS.

Simulation	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
g_4 (T/m)	22.1	21.5	20.9	20.3	19.7	19.1	18.5	17.9	17.3	16.7	16.1	15.5	14.9	14.3	13.7
dose peak position (cm)	4.09	4.99	6.21	7.12	8.33	5.54	11.05	12.57	14.08	15.06	17.42	19.24	21.66	23.78	26.51

15.2.2 SOEP Optimization Algorithm

The following steps were implemented using the Python programming language [Python Software Foundation 2023]. Output files from the 15 simulations, where focal positions were distributed along the phantom's depth, were preprocessed to extract the PDDs, denoted as $d_1(z)$, $d_2(z)$, ..., $d_{15}(z)$, along with their respective standard deviations, $s_1(z)$, $s_2(z)$, ..., s_{15}

(z). These values are expressed as percentages of the deposited doses at each computed position z , providing information on their uncertainties. Upon user-defined selection of a region of interest (ROI) between depths $z_{\min} \leq \text{ROI} \leq z_{\max}$, representing the tumor region, the PDDs whose dose deposition peaks fall within this ROI are chosen. To achieve broader dose coverage in the tumor, the user can also define a tolerance z_{tol} , extending the PDD selection to the region $z_{\min} - |z_{\text{tol}}| \leq \text{ROI} \leq z_{\max} + |z_{\text{tol}}|$. After the selection, the algorithm pre-normalizes the chosen $d_i(z)$ curves by multiplying them by coefficients a_i , where the values ensure that the peak dose of each curve is equal to that of the curve with the maximum peak dose before pre-normalization. Following this step, the algorithm performs the weighted sum $D(z)$ of the selected curves,

$$D(z) = \sum_{i=1}^n a_i d_i(z) \quad (1)$$

where the coefficients a_i can be interpreted as the number of times that $d_i(z)$, the i -esim PDD is added to the weighted sum $D(z)$. These coefficients will be optimized to achieve an optimal SOEP, with a high and homogeneous dose along the selected ROI.

The optimization process utilizes the minimize function from the `scipy.optimize` library [Virtanen et al. 2013], employing the Powell minimization method, which allows for addressing minimization problems while adhering to predefined constraints [Scipy Developers 2023]. Establishing lower and upper bounds (*bounds*) for the coefficients during the optimization prevents the occurrence of non-physical results, such as, for example, negative combined doses, and impractical extremes as well. The pre-normalized coefficients a_i are used as the initial estimates, required by the selected method to determine the optimal coefficients b_i (i.e., initially, $b_i = a_i$). Additionally, to ensure stability and physical relevance, the optimization constraints limit the coefficients b_i to vary between one and ten times their initial values (i.e., $a_i \leq b_i \leq 10 a_i$).

In a mathematical optimization problem, the objective function is an expression representing the value to be minimized or maximized within the set of feasible alternatives. This function encapsulates the fundamental objective of the problem, guiding the search for the ideal solution [Overview of optimization 2006]. Since this work aims to achieve a plateau (SOEP) with high dose deposition and low variation within the specified ROI, the

chosen objective function is the ratio of the standard deviation to the mean of the dose deposited in the SOEP. In other words, we are minimizing the coefficient of variation (CV) of the dose within the ROI. In Eq. 1, substituting a_i with b_i and limiting the values of z within the ROI, the weighted sum of the dose in this region, $D_{ROI}(z)$, is obtained,

$$D_{ROI}(z) = \sum_{i=1}^n b_i d_i(z) \quad , \quad z_{\min} \leq z \leq z_{\max} \quad (2)$$

Calculating the average dose and the standard deviation of the dose within the ROI, denoted respectively by \bar{D}_{ROI} and s_{ROI} ,

$$\bar{D}_{ROI} = \frac{1}{m} \sum_{j=1}^m D_{ROI}(z_j) \quad , \quad s_{ROI} = \sqrt{\sum_{j=1}^m \frac{[D_{ROI}(z_j) - \bar{D}_{ROI}]^2}{m-1}} \quad (3)$$

these quantities are used to calculate the objective function to be minimized,

$$F_{obj} = CV = \frac{s_{roi}}{\bar{D}_{roi}} \times 100 \quad (4)$$

In each iteration, the algorithm finds the set of coefficients b_i whose values minimize F_{obj} as follows,

$$\mathbf{b} = \underset{b_1, b_2, \dots, b_n}{arg \min} \{F_{obj}(\mathbf{b})\} \quad , \quad a_i \leq b_i \leq 10a_i \quad , \quad i = 1, 2, \dots, n, \quad (5)$$

where the representation of the vector \mathbf{b} is a list of values, and each element b_i is the resolution corresponding to the optimization problem for the current iteration,

$$\mathbf{b} = [b_1, b_2, \dots, b_n] \quad (6)$$

The optimal values obtained for the coefficients, stored in \mathbf{b} , are then automatically applied to the weighted sum $D_{ROI}(z)$. The minimization is performed sequentially, iteratively, and the optimized coefficients can vary from one iteration to another. This approach allows dynamic adaptation of the coefficients throughout the optimization process, responding to

changes in conditions or problem requirements, resulting in a more efficient search for the optimal solution.

Once the optimal coefficients b_i have been obtained, the standard deviation of the weighted sum, $S(z)$, is calculated as follows,

$$S(z) = \sqrt{\sum_{i=1}^n b_i s_i^2(z)} \quad (7)$$

where $s_i(z)$ are vectors containing the standard deviations associated with the selected PDDs, $d_i(z)$. To avoid the risk of undersizing $S(z)$, the values b_i are rounded up in Eq. 7. After performing the calculation described in Eq. 7, the code returns the highest percentage standard deviation from the combined mean computed in the ROI interval, $S_{ROI^*} = \arg \max\{S_{ROI}(z)\}$. This quantity is used to estimate the upper bound of the 99.73% confidence interval associated with the SOEP obtained after the optimization of the weighted sum $D_{ROI}(z)$.

$$IC_{99,7}^{*} = \pm 3S_{ROI}^{*} \quad (8)$$

15.3 Results and Discussion

Fifteen simulations were carried out with the configurations described in Table 1. The non-normalized PDDs obtained from these simulations are illustrated in Figure 2, being numbered from the highest to the lowest magnetic field gradient, corresponding to an increasing order in the electron beam focal position. The chosen values for the gradient g_4 , associated with the last quadrupole q_4 , have increments of 0.6 T/m. This choice resulted in PDD peaks separated by an average distance of 1.6 cm, distributed between approximately 4 cm and 27 cm of depth along the phantom.

After the user defines the ROI and z_{tol} , the algorithm selects the focused PDDs within these limits. In all cases presented in this study, a z_{tol} of 2 cm was used to test the algorithm's functionality. However, in a real application, the definition of z_{tol} will depend on the presence of healthy organs adjacent to the ROI, as this could imply the need to apply a tolerance close to zero, or the choice of different g_4 values, thus obtaining additional focal positions that allow the attainment of an appropriate SOEP.

Figure 2. PDDs from 15 simulations performed with the same VHEE beam, with distinct focal positions distributed along the phantom, obtained by varying the magnetic field gradient of the fourth quadrupole (g_4) as indicated in Table 1.

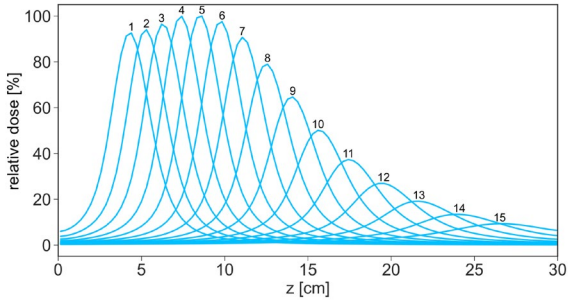
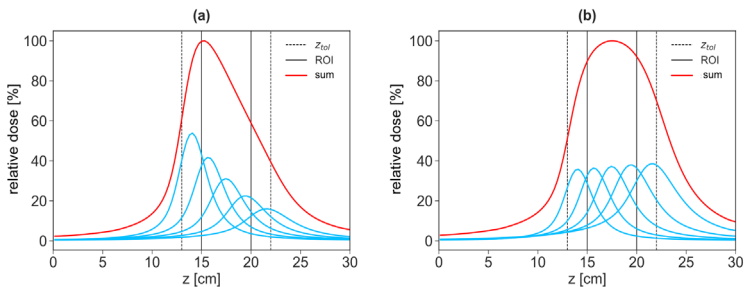


Figure 3 (a) illustrates the non-normalized PDDs (blue lines) selected for a ROI between 15 and 20 cm, with a z_{tol} of 2 cm, along with their summation (red line). Figure 3 (b) shows the selection and summation of these PDDs after the pre-normalization described in Equation 1. Comparing both panels, it can be observed that the dose profile in the ROI in Figure 3 (b), while not yet flat, exhibits symmetry and reduced variation compared to the dose profile in Figure 3 (a). Normalizing the amplitudes of the selected PDDs through pre-normalization brings the profile of the weighted sum closer to the desired profile (SOEP plateau). Thus, using the coefficients a_i as initial estimates for the values of the coefficients b_i (to be optimized) reduces the number of iterations required to complete the optimization process, making the attainment of the optimal SOEP more efficient.

Figure 3. Pre-optimization process, showing the selection and summation of curves with peaks in the ROI $\pm z_{tol}$ (a) before and (b) after pre-normalization.



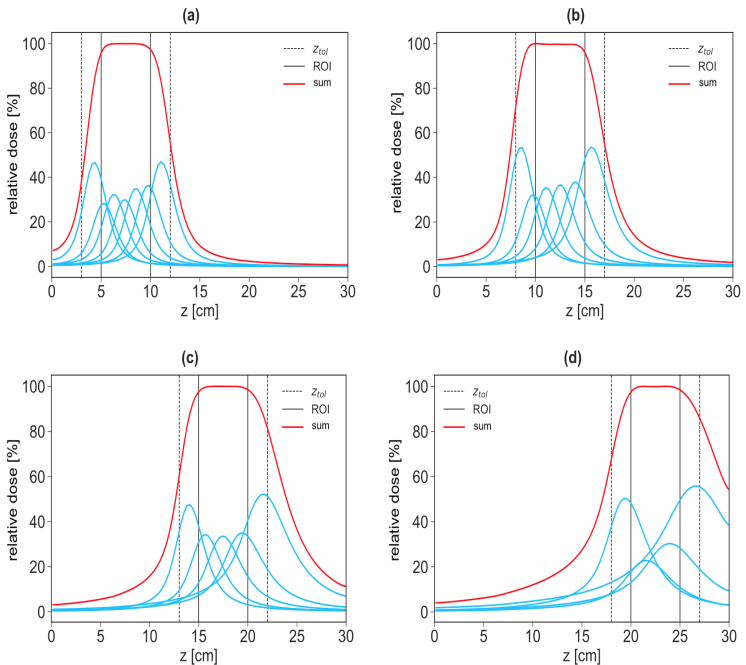
The SOEPs obtained after the coefficient optimization using the Powell method for four distinct ROIs (5 to 10 cm, 10 to 15 cm, 15 to 20 cm, and 20 to 25 cm) are illustrated in Figure 4. The optimization results, including the optimal values of the coefficients, the objective function values, and the largest values of the confidence intervals associated with the obtained profiles, are listed in Table 2. As the number of selected curves depends on the quantity of PDDs available within the chosen ROI, the number of coefficients shown in the table for each optimization varies. Regarding the values of the objective function obtained in each optimization, since this function is the coefficient of variation of the dose in the ROI, they can be used as direct measures of the quality of the obtained SOEPs. For all considered ROIs, $F_{obj} \approx 0.2\%$. In other words, in all four evaluated cases, the standard deviation of the dose along the ROI was only 0.2% of the average dose obtained in the SOEP, highlighting the effectiveness of the proposed algorithm for its optimization. To assess the uncertainty of the dose obtained from the weighted sum of the selected PDDs in each optimization, the largest values of the confidence intervals ($CI_{99.7}^*$) associated with these profiles are also included in Table 2. For the ROIs displayed in panels (a), (b), (c), and (d) of Figure 4, the values of $CI_{99.7}^*$ were, respectively, $1.2 \times 10^{-05} \%$, $8.3 \times 10^{-06} \%$, $8.9 \times 10^{-06} \%$, and $9.9 \times 10^{-06} \%$. Although these values are approximately an order of magnitude larger than the values associated with individual PDDs, they are still very small and cannot be accurately represented graphically in the figure panels.

The panels in Figure 5 illustrate two-dimensional dose profiles (axes y and z , in a cross-section at coordinate $x = 0$) corresponding to the optimized weighted sums obtained for the same ROIs shown in Figure 4. The panels in Figure 5 show reasonably localized and homogeneous dose profiles along the ROIs. However, they also highlight an increase in the width in y of these profiles as the ROI is shifted to greater depths in the phantom.

Table 2. Optimized weighting coefficients by the algorithm using the Powell method for the SOEPs in Figure 4 in a single run to minimize the objective function and maximize the confidence interval values of each SOEP.

ROI (cm)	b_1	b_2	b_3	b_4	b_5	b_6	b_7	F_{obj} (%)	$IC_{99,7}^*$ (%)
5 to 10	1.8	1.1	1.2	1.1	1.2	1.3	1.8	0.2	1.2×10^{-05}
10 to 15	1.7	1.0	1.2	1.5	1.8	3.4	-	0.2	8.3×10^{-06}
15 to 20	1.7	1.6	2.1	3.0	6.2	-	-	0.2	8.9×10^{-06}
20 to 25	2.6	1.7	3.2	8.4	-	-	-	0.2	9.9×10^{-06}

Figure 4. Optimized SOEP using the Powell method for ROIs defined in (a) from 5 to 10 cm, (b) from 10 to 15 cm, (c) from 15 to 20 cm, and (d) from 20 to 25 cm. In all cases, Z_{tot} is 2 cm.



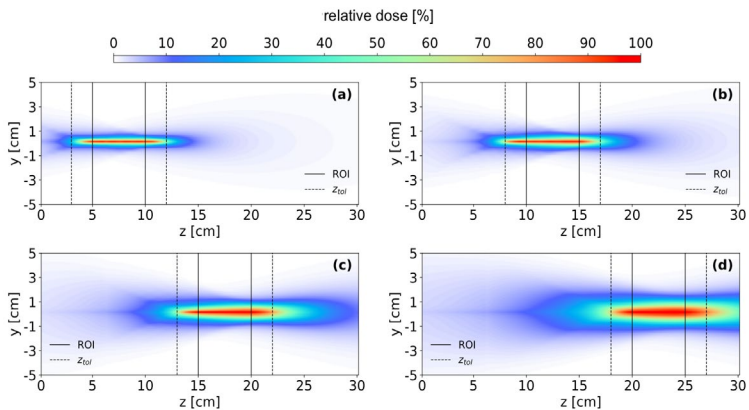
The optimizations presented so far were performed using the Powell method, which allows the definition of constraints such as the bounds adopted in this work for the values of the optimized coefficients. Since the minimize function from the scipy.optimize library has other methods that

also accept such constraints, it is worthwhile to compare them. Table 3 lists the results of optimizations carried out for the ROI of 20 to 25 cm with the L-BFGS-B, trust-constr, SLSQP, and TNC methods, all of which accept the adopted limit definition. To facilitate comparison, the results obtained with the Powell method, listed in Table 2, have been repeated in this table. Table 3 shows that all methods reached the same minimum value for the objective function, $F_{obj} = 0.2\%$, with practically equivalent confidence intervals. Regarding the optimized coefficients, the trust-constr method returned relatively higher values than the others. However, when normalized by their first values ($b_i \leftarrow b_i / b_1, i = 1, \dots, 5$), the sequences of coefficients provided by the different methods are practically identical, indicating reasonable equivalence between the evaluated minimization methods.

Table 3. Coefficients of the weighted sum of selected PDDs for the ROI of 15 to 20 cm, optimized by different methods to minimize the objective function in obtaining the SOEP.

Method	b_1	b_2	b_3	b_4	b_5	F_{obj} (%)	$IC_{99,7}^*$ (%)
Powell	1.7	1.6	2.1	3.0	6.2	0.2	8.9×10^{-06}
L-BFGS-B	1.5	1.4	1.8	2.6	5.4	0.2	9.7×10^{-06}
trust-constr	4.4	4.1	5.4	7.7	16.2	0.2	5.3×10^{-06}
SLSQP	1.5	1.4	1.8	2.6	5.4	0.2	9.7×10^{-06}
TNC	1.5	1.3	1.8	2.6	5.5	0.2	9.7×10^{-06}

Figure 5. Transverse dose profiles for each Powell-optimized SOEP for the ROIs of (a) 5 to 10 cm, (b) 10 to 15 cm, (c) 15 to 20 cm, and (d) 20 to 25 cm.



15.4 Conclusions

This study proposed an algorithm that optimizes the weighted sum of a selected set of PDDs, obtained from Monte Carlo simulations performed in TOPAS for the same VHEE beam, focused at positions distributed along the depth (coordinate z) of a given phantom. The selection of PDDs to be summed is based on the ROI defined by the user, and the optimization aims to obtain the coefficients (weights) of the weighted sum that minimize the coefficient of variation of the resulting PDD curve in the selected ROI. The result of this process is the formation of a SOEP, a plateau of maximum dose that is homogeneous along the selected ROI.

The use of the algorithm was exemplified in four distinct ROIs, demonstrating its functionality in selecting PDDs and optimizing the coefficients of their weighted sums at different depths of the phantom. In all cases, the algorithm was able to generate highly homogeneous SOEPs, with coefficients of variation on the order of only 0.2% of the average doses in the ROIs, and with percentage uncertainties on the order of 10^{-6} . From the bidimensional dose profiles (axes y and z , at $x = 0$) of the optimized weighted sums in obtaining these SOEPs in these four ROIs, it was possible to observe that the transverse width (y -axis) of the dose distribution increases as deeper ROIs are selected. Different minimization methods available in the selected optimization library were tested, presenting very similar results and behaviors.

Despite the positive results obtained in this study, it was limited to minimizing dose variation along the z coordinate (depth) of the phantom, using only PDDs as input data for the developed algorithm. In a future work, the algorithm's application will be extended to a volumetric ROI, with the option of multiple irradiation fields. The addition of such features will enhance the algorithm's applicability, potentially contributing to the development of a treatment planning system for focused VHEE radiotherapy. Another limitation of the current algorithm is that it always uses all selected PDDs in the ROI to obtain the optimized profile. In a future version, we intend to implement the verification of the minimum number of PDDs needed to form a homogeneous SOEP. Since each PDD in the weighted sum requires an adjustment of the VHEE beam focus, reducing the number of PDDs used in the weighted sum would simplify and expedite VHEE radiotherapy operations. An algorithm with the listed improvements could be implemented in the calibration and use of future focused VHEE radiotherapy equipment, streamlining and automating the steps necessary

to achieve the best dose distribution in a given tumor volume.

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16 Optimizing Laser-Plasma Accelerators for Medical Radioisotope Production

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Abstract:

Radiopharmaceuticals, used in nuclear medicine, are formed by drugs and radioisotopes, the latter being mainly produced by nuclear fission of highly enriched uranium, which produces a large amount of radioactive waste. A promising alternative for producing ^{99}Mo , which decays to $^{99\text{m}}\text{Tc}$ – the most used radioisotope in nuclear medicine – without relying on uranium fission, is photoactivation via laser-plasma accelerators. In light of these factors, this work proposes using Bayesian optimization in particle-in-cell simulations of a symmetric gas target for a laser-plasma accelerator, to enhance the radioisotope ^{99}Mo yield. To produce Gaussian pulses with a length of $15\ \mu\text{m}$ (50 fs) and $7\ \mu\text{m}$ in waist radius, a laser with a peak power of 5 TW was chosen, operating with high repetition rates in the self-modulated regime. It was possible to obtain an electron beam with a charge of 544 pC, 15.1 MeV of median energy, and 59 MeV of maximum energy, all considering electrons above the threshold of 8 MeV, for producing of bremsstrahlung photons to photoactivate the nuclear reaction to generate the ^{99}Mo .

Keywords: Bayesian optimization, particle-in-cell simulation, laser-plasma acceleration, photoactivation, electron beam.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure; 12. Responsible Consumption and Production.

16.1 Introduction

16.1.1 Radioisotopes in nuclear medicine

The clinical scenario in health centers is characterized by the need to use technologies capable of diagnosing and treating illnesses, such as neurological and cardiac diseases and certain types of cancer [IAEA, 2017]. For this purpose, nuclear medicine, a specialized medical field, employs radiopharmaceuticals that can be administered to patients either intravenously or orally. [SHNEIDER, 2005].

Radiopharmaceuticals are radioisotopes linked to medicines, and each organ will capture and metabolize these radioactive compounds in a specific way. In this way, radiopharmaceutical allows the observation of physiological functions and metabolic activity, as well as exploring the health of organs individually and promoting their treatment [IAEA, 2017]. This feat is possible due to the emission of radiation (electromagnetic and/or corpuscular waves) from the specific location at which the radiopharmaceutical is fixed in the human body [ELISA, 2018].

In general, for diagnostic purposes, radioisotopes that emit β^+ particles and/or γ rays are used, while, for therapy, radioisotopes that emit Auger electrons and β^- particles are administered. Considering a global scope, Technetium-99m (^{99m}Tc , half-life of 6h) is the most used, mostly being applied in scintigraphy procedures [World Nuclear Association, 2023].

^{99m}Tc is produced in $^{99}\text{Mo}/^{99m}\text{Tc}$ generators, while ^{99}Mo (half-life of 66h) is mainly produced in nuclear reactors through the fission of highly-enriched uranium (^{235}U) [IAEA 2001], which results in the formation of different radioisotopes, including ^{99}Mo (~6% of the yield [ZOLLE, 2007]. However, this method has several aggravating factors, the main ones being the generation of radioactive waste (especially the radioisotopes with long decay times) [World Nuclear Association, 2023], the need to transport highly radioactive material over long distances [CHO, 2010], and the elimination of highly-enriched uranium due to international nuclear non-proliferation policies [National Research Council, 2009]. Therefore, it is necessary to encourage research aimed at exploring alternatives to uranium-based production methods to find more ecological solutions that meet the growing demand for ^{99m}Tc .

16.1.2 Laser wakefield accelerators and photoactivation

A promising alternative for producing the radioisotope ^{99}Mo without the need for radioactive uranium and, consequently, excluding the aforementioned challenges, is by photonuclear reactions (photoactivation). In particular, the $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ reaction route has a high cross-section for photons with energies between 8 MeV and 20 MeV, peaking at approximately 14.5 MeV. Bremsstrahlung photons with energies within this range could be generated by impinging an SM-LWFA-accelerated electron beam in a tantalum (Ta) converter, positioned prior to a Mo target. For this application, low-quality electron beams, with high divergence and energy spread, may suffice, provided they can generate a high flux of bremsstrahlung photons. Such beams could be produced using compact laser wakefield accelerators (LWFA), capable of providing acceleration gradients in the order of hundreds of GeV/m [TAJIMA, 1979; ESAREY, 2009]. Moreover, modern laser systems, with peak powers ranging from 1 TW to 10 TW could be used to build laser wakefield accelerators in the self-modulated regime (SM-LWFA) [KRALL, 1993; FISHER, 1996; MALDONADO, 2021], operating at repetition rates of a few kHz [ROVIGE, 2020].

16.1.3 Particle-In-Cell Simulations and Bayesian Optimization

Despite impressive experimental results, LWFA technology is still under development. Hence, there is currently no straightforward methodology to address the complexity and instabilities that arise from the intricate, nonlinear laser-plasma coupled dynamics. One way to simulate and understand the phenomena of laser-plasma electron acceleration is through particle-in-cell (PIC) simulations, which can describe the self-consistent dynamics of charged particles in electromagnetic fields. However, due to the high computational cost of PIC simulations, and the large parameter space associated with the laser and plasma characteristics that will determine the acceleration of electrons in an SM-LWFA, conventional parameter scans – in which a large number of simulations are executed to cover a vast grid of possible combinations – is not an efficient approach. On the other hand, Bayesian Optimization, which is an algorithm capable of optimizing non-trivial multidimensional functions [BROCHU, 2010], may be an excellent alternative for this purpose [JALAS, 2021]. By using Bayesian optimization, the input values to be adopted in the next PIC simulation are determined by the algorithm, based on the previous existing results, aiming to maximize an objective function based on the desired

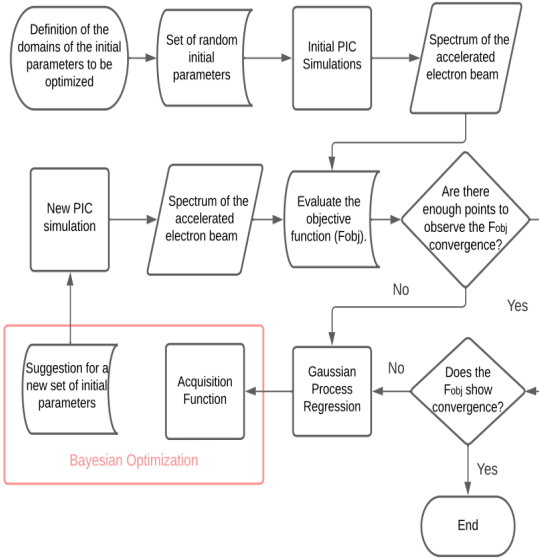
LWFA output properties such as the energy and charge of the LWFA-accelerated electron beam.

Enabling the production of ^{99}Mo via LWFA-accelerated electrons (rather than using highly-enriched uranium for this purpose) would have a positive impact on the environment, allowing the improvement of quality of life and health by using and producing resources responsibly, as well as promoting innovation in this industry, these being crucial points in UN sustainable development goals [UN, 2018]. Thus, to make plausible the attainment of an electron beam with the necessary characteristics to enable the production of the radioisotope ^{99}Mo via photoactivation, this chapter aims to determine the optimal parameters of a laser-driven plasma accelerator using the Bayesian Optimization algorithm, based on data from PIC simulations.

16.2 Optimization of a Symmetric Trapezoidal Gas Profile

The workflow of this work is depicted in Figure 2.1. As an initial step, a database is formed, initiating the optimization algorithm from a set of results from PIC simulations executed with input parameter values randomly chosen within their previously determined variation ranges. The objective function value is then calculated using the output parameters of each PIC simulation, in this case, obtained from the energy spectrum of the accelerated electron beam. Based on the available data points, the objective function is approximated using a probabilistic model, in this case, Gaussian process regression (GPR), enabling the use of Bayesian optimization. The acquisition function, computed from GPR parameters, determines the next set of input parameters to be sampled. Each iteration of the optimization process generates the initial condition (a set of input parameters) for a new PIC simulation, whose results will be used to calculate the objective function and update the database. This loop is repeated until convergence – of the objective function, around the highest observed values – is attained.

Figure 2.1. Flowchart of the Bayesian optimization process, coupled with PIC simulations.



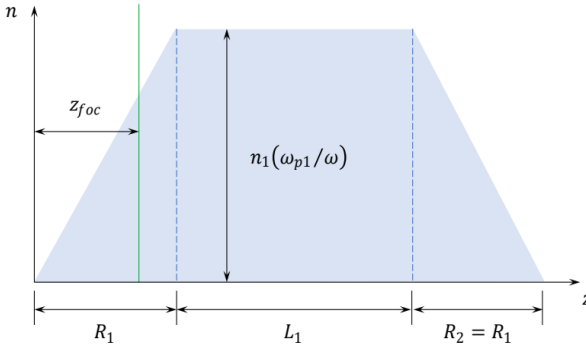
The Fourier-Bessel Particle-In-Cell (FBPIC) code [LEHE, 2016] was employed in this study. It is developed in the Python programming language and utilizes a cylindrical grid, which is suitable for the laser pulse envelope due to the inherent symmetries in this coordinate system. Simulations were conducted on the Santos Dumont Supercomputer at the Laboratório Nacional de Computação Científica (LNCC). To avoid excessive disk space usage, only two files were saved per simulation during the Bayesian optimization process, with the first file saved at the initial simulation time and the second file recorded at the final time.

A crucial step for the application of Bayesian optimization is the definition of an objective function. In order to establish a connection between the initial quantities in PIC simulations and the resulting electron beam in each simulation, the objective function was defined as

$$F_{obj} = \max \sum_i^{N_{bins}} E_i Q_i, \quad E_i > 8 \text{ MeV},$$

where E_i [MeV], Q_i [nC], and N_{bins} are, respectively, the energy, the total charge of particles with that energy, and the number of bins in the histogram (energy spectrum) of the accelerated beam. In this work, $N_{bins} = 200$ was adopted. Among the available kernels, the Matérn kernel with the parameter ν (\mathbf{v}), which controls the smoothness of the learned function, was employed with a value of 2.5. The upper confidence bound was defined as the acquisition function. Ten initial random simulations were performed. The target gas was H_2 , with the symmetric trapezoidal profile presented in the work of Maldonado et al. This profile, illustrated in Figure 2.2, can be understood as a linear approximation of a Gaussian profile.

Figure 2.2. Initial gas density profile before ionization, with the focal position of the laser pulse represented by the green line.



For the simulation, the following values were employed for the laser pulse: peak power $P = 5$ TW, Gaussian beam with a longitudinal length (FWHM) $c\tau = 15 \mu\text{m}$, and waist radius $r_0 = 7 \mu\text{m}$. The laser was simulated to impinge on a gas with the profile shown in Fig. 2.2, which has a maximum density n_1 on the plateau, and up- and down-ramps with fixed horizontal lengths, $R_1 = R_2 = 80 \mu\text{m}$. As shown in Table 2.1, three input parameters were varied: the ratio between the plasma and laser angular frequencies, ω_{p1} / ω , the plateau length, L_1 , and the laser focal position, z_{foc} . Each combination of these parameters creates an electron beam with specific characteristics. Table 2.1 also displays the variation ranges (intervals) of these input parameters, chosen based on previous existing studies of SM-LWFA [MALDONADO, 2021].

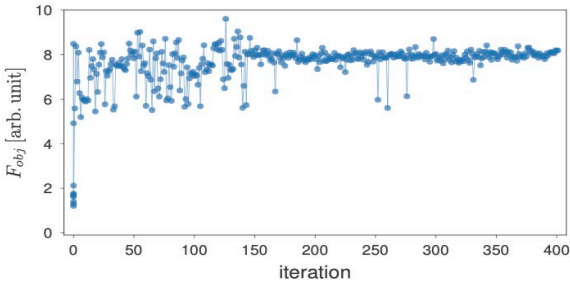
Table 2.1. List of input parameters and their variation intervals.

Parameter	Interval	Unit	Description
ω_{p1}/ω	0.15 , 0.40	–	Plasma and laser frequencies ratio at the plateau
L_1	30 , 60	μm	Plateau length
z_{foc}	30 , 60	μm	Laser pulse focal position

16.2.1 Results and discussion

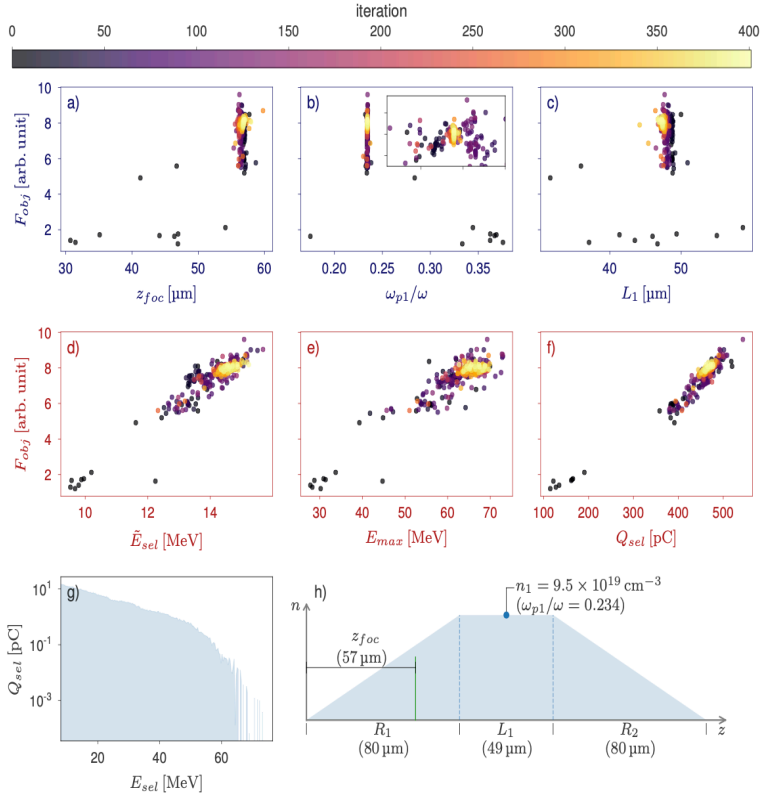
Bayesian Optimization was applied using the Botorch package, which converged after approximately 150 iterations around $F_{obj} \approx (7.9 \pm 0.3)$ arb. unit, as shown in Figure 2.3. The non-convergence to the highest value attained, $F_{obj} \approx 9.6$ arb. unit, at iteration 135, can be explained by the significant impact of small variations in the initial parameters on the objective function output. Figure 2.4 summarizes these factors.

Figure 2.3. Evolution of the objective function (F_{obj}) along the iterations of the optimization algorithm. Convergence around (7.9 ± 0.3) arb. unit is observed after approximately 150 iterations.



Analyzing Figure 2.4, rapid convergence is observed for the laser focal position ($z_{\text{foc}} \approx 57 \mu\text{m}$), the ratio between plasma and laser angular frequencies (with fine-tuning in this parameter), and the plateau length ($L_1 \approx 47.5 \mu\text{m}$). Figure 2.4(d) highlights the convergence towards an electron beam with a median energy of $\bar{E} \approx 14.5 \text{ MeV}$. Additionally, in panel (e), convergence is observed for a range of maximum particle energies with $64 \text{ MeV} < E_{\text{max}} < 70 \text{ MeV}$, and in image (f), convergence is seen for the total charge selected in the range of $450 \text{ pC} < Q_{\text{sel}} < 500 \text{ pC}$, with a value of $Q_{\text{sel}} \approx 550 \text{ pC}$ for the highest F_{obj} attained along the optimization. Finally, the lower panels, Figures 2.4(g) and (h), depict the optimal energy spectrum and gas-density profile.

Figure 2.4. Summary of results. Scatter plots of the objective function compared to (a) the laser focal position (z_{foc}), (b) plasma and laser frequencies ratio (ω_{p1}/ω), (c) plateau length (L_1), (d) median energy above 8 MeV (\bar{E}_{sel}), (e) maximum energy (E_{max}), and total charge above 8 MeV (Q_{sel}). Additionally, panels (g) and (h) show the optimal energy spectrum and gas-density profile, respectively. The optimal values for the input parameters are indicated in panel (h) as well.



16.3 Conclusion and Future Directions

The objective of this work was to obtain an electron beam capable of generating photons with sufficient energy to produce the radioisotope ^{99}Mo through the $^{99}\text{Mo}(\gamma, n)^{100}\text{Mo}$ reaction pathway, using a Bayesian optimization algorithm based on PIC simulations. With the application of the algorithm in the described case, it was possible to achieve an electron beam

with a charge of 544 pC, a median energy of 15.1 MeV, and a maximum energy of 59 MeV, considering the 8 MeV threshold for bremsstrahlung photon production via photoactivation.

In future works, the intention is to use the optimal spectrum obtained in the TOPAS code to simulate the production and activity of the ^{99}Mo radioisotope. Additionally, it is worthwhile to explore different profiles, such as asymmetric trapezoidal profiles, given the influence of various plasma density regions on the dynamics of these systems.

16.4 Acknowledgments

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17 Digital Health and mHealth Solutions: Application Cases

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Abstract:

Digital health solutions are rapidly transforming healthcare delivery, addressing the needs of both healthcare professionals and patients. A major challenge for healthcare organizations is managing patient data and effectively monitoring patients, especially in high-burden settings. mHealth solutions offer promising tools to address these challenges, potentially increasing productivity and reducing risks. This chapter describes two mHealth application models developed by students in the Graduate Program in Health Information Technologies and Management. The first model, "Digital Vaccine Card BR," is a mobile application designed to improve vaccination coverage rates in Porto Alegre, Brazil. The second model, "@MoreDigitalLife", is a mobile application intended to support the post-discharge care of elderly patients from a complex care hospital in the same city. Applied studies were conducted to evaluate the effectiveness of these mHealth solutions. The studies demonstrated that both applications have the potential to significantly improve communication and connection between patients and healthcare managers.

Keywords: Digital Health; Mobile Health; Applications Cases on Health
Sustainable Development Goals (SDG): 3. Good Health and Well-being; 10. Reducing inequalities.

17.1 Introduction

The World Health Organization (WHO) defines “mHealth” or “mobile health” as a term used for medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, Personal Digital Assistants (PDAs), and a variety of wireless devices. mHealth applications can include the use of mobile devices in collecting community and clinical health data, delivery of healthcare information to health professionals and patients, including real-time monitoring of patient vital signs, and direct provision of care (WHO, 2015).

As reported in the WHO (WHO, 2018) reports, countries have implemented digital health policies and national strategies, reaching a level of more than 63%. In this way, it is clear that digital health is in the process of transforming the entire health sector and the way health care is provided, noting that digital health solutions can increase access to health services, provide training to healthcare professionals, empower patients, provide better diagnoses and health information to the individual. The subject has high international relevance, which led to the creation, through the aligned approval of the International Telecommunication Union (ITU) and WHO, of the National E-Health Strategy Toolkit (ITU, 2016).

MHealth can be understood as an element of Electronic Health (eHealth), as part that addresses the use of Information and Communication Technologies in the health area, a field that has the potential to provide innovative solutions to well-being issues (ALLIDA et al., 2020).

In the context of mHealth, patient monitoring or tracking is defined as the use of technology to manage, monitor, and treat a patient's illness remotely (e.g., diabetes or heart patients). Remote sensors installed in homes or imaging devices attached to mobile phones are often used to facilitate data transmission to the healthcare provider. It can reduce the need for visits to a health center or professional for check-ups (WHO, 2011). The greatest benefits of using mobile devices for health are the fact that these devices are personal and intelligent with processing capacity, in addition to having Internet connectivity and being portable (WHITTAKER et al., 2012).

The objective of this chapter is to describe two mHealth application models that allowed the addition of the main functionalities required: a) support vaccination coverage in the city of Porto Alegre and evaluate the proposed model with health professionals in the city; b) support the care of

elderly people post-discharge from a hospital in the city of Porto Alegre. Both models were designed and evaluated with the contribution of health professionals involved in both scenarios. It is noteworthy that the projects that gave rise to the research were approved by the appropriate Ethics Committees involved. In this sense, this chapter discusses the importance of using mHealth solutions and the technologies involved as resources for promoting health surveillance and health well-being, as well as assistance in health management.

17.2 Theoretical foundation

17.2.1 Vaccination and Information Technology

The current Brazilian immunization policy has its origins in the sixties, with the creation of the National Immunization Program (PNI), motivated by the smallpox eradication campaign (TEMPORÃO, 2003). The PNI distributes more than 300 million doses per year of 44 different immunobiologicals, including vaccines, serums and immunoglobulins. It has approximately 34 thousand vaccination rooms and 42 Special Immunobiological Reference Centers (CRIE), which serve individuals with special clinical conditions. The PNI uses different vaccination strategies, including routine vaccination, campaigns, vaccine blocks and extramural actions (BRASIL, 2018). Since its creation, the PNI has adopted an integrated vision of immunization (BENCHIMOL, 2001), covering the entire society, including indigenous and prison populations. The Program provides for the installation of laboratories, management of dose administration techniques and health education actions (HOCHMAN, 2011).

One of the pillars of support for the PNI are the vaccination campaigns which, in a certain way, are responsible for spreading the culture of vaccination in Brazil. However, in recent years the government has encountered difficulties in achieving certain immunization coverage and several campaigns have been prolonged to achieve the goals established by the Ministry of Health, making it common for people not to seek out health units within the established deadline, relying on the extension of the term. An example is the 2013 flu vaccination (BACURAU; STOLSES; FRANCISCO, 2018).

In partnership with the SUS Department of Informatics (DATASUS), a department of the Ministry of Health, the National Immunization Program Information System (SI-PNI) was built. All information collected by the system helps in making decisions to be used by the program.

Technologies such as digital health are useful tools for scheduling vaccinations, unique user identification, searching for health system users who do not return to complete vaccination schedules, providing scientific information, clinical guidance, locating stations and opening hours, integration of health professionals and the community, in addition to monitoring vaccination coverage for the population.

17.2.2 Elderly and Gerontechnology

The healthy aging of the population is a concern for all governments since longevity has increased significantly. The elderly represent a significant part of the population and have limitations and weaknesses imposed by the natural and biological aging of the human body. Elderly people who require hospital services who are admitted to hospital need continuity of care after hospital discharge. This care is a topic present in the private and public network, aiming to promote user participation and decision-making, as well as enabling safe, coordinated, efficient and effective transitions for the care of elderly patients (GOMES et al., 2021).

Gerontechnology, with the support of digital technologies, can assist healthcare professionals in post-discharge monitoring of the elderly, offering relevant solutions, depending on the needs of each patient.

The Brazilian Society of Gerontechnology explains that this area consists of combining gerontology with technology to guarantee health, full social participation and independent life throughout the aging process. Therefore, its main objective is to understand the needs of older people and communicate them to a broader community (SBGTEC, 2022).

17.3 Method

The studies conducted were of an applied and exploratory nature, and of technological production. They are single case studies designed for the reality of situations relating to the municipality of Porto Alegre. They were based on the User-Centered Design model (Wardhana et. al., 2017), using the steps: analysis/design and conceptual development, and definition of the relevance of features and results.

The methodological steps included: 1) Literature review on the topics covered in each mHealth solution; 2) Identification of functional and non-functional requirements with the support of interviewed health professionals; 3) Mapping of mHealth solutions available on public platforms with functionalities similar to those intended for the project; 4)

Definition of the desired functionalities and the information architecture to be implemented in the mHealth solution; 5) Selection of low/no code platform for prototype development; 6) Development of the Digital Vaccine Card BR and @More Digital Life prototypes; 7) Verification and evaluation of the prototype by healthcare professionals regarding the features available with the main focus on usability; 8) Analysis of results. The platforms used to develop mHealth solutions were respectively FabApp ¹ and Figma², due to their ease of use by students in the interdisciplinary area.

17.4 Applications Cases

Following this chapter, two mHealth solutions developed in research in the Graduate Program in Information Technologies and Health Management, and integrated into the Intelligent Systems Applied to Health Research Group³ will be described. The first application refers to the solution designed to support vaccination coverage in the city of Porto Alegre, and the second solution designed to support the care of elderly people post-discharge from a hospital in the city of Porto Alegre. The solution's interfaces were developed with information in Portuguese, so it was decided to keep the interfaces as designed in the models in this chapter.

17.4.1 mHealth For Vaccination Follow-Up for Brazilian

The model Digital Vaccine Card BR (in Portuguese, Carteira Digital de Vacinas BR) aims to encompass the main functionalities necessary for vaccination coverage in the city of Porto Alegre. The application model was designed through a survey of functional and non-functional requirements for the mHealth solution, together with health professionals who work directly with vaccinations at the Porto Alegre Municipal Health Department. The application was developed for mobile devices and web platforms, compatible with iOS and Android operating systems. Both patient users and healthcare professional users can use it. After registering, with their respective identifying documents (Individual Registration or Professional Registration), the user will be able to continue using the application, whether for recording information, consultations, reports, research, vaccination history, donations, allergies, comorbidities, traceability and

¹ <https://fabricadeaplicativos.com.br/en>

² <https://www.figma.com/>

³ <https://dgp.cnpq.br/dgp/espelhogrupo/2437746416727738>

location from the nearest health unit. The solution was modeled on the Fabapp Platform, a platform that allows modeling based on information architecture defined with no code.

Figure 1. Digital Vaccine Card BR' interfaces: (a) main interface and (b) menu of options.

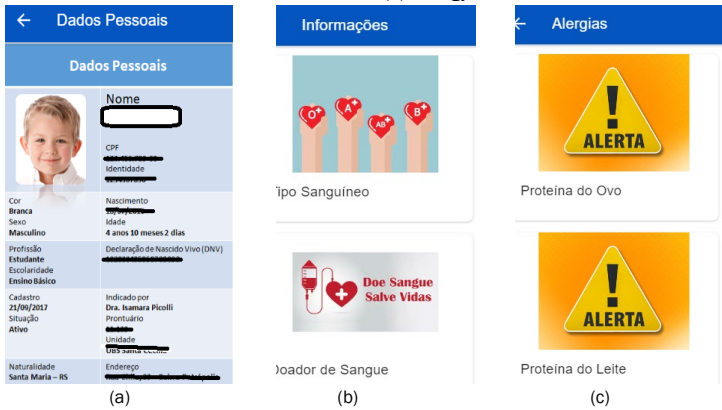


Source: Author.

Figure 1 presents the mHealth solution's presentation interface and the options menu, where the user's vaccination card is located, the vaccination calendar published by the Ministry of Health, vaccination campaigns also find space in the solution, as well as information for travelers health services in other countries, epidemic alerts, a list of service stations with the vaccines offered, links with accessible information/communications from scientific literature and finally, a space with Frequently Asked Questions (FAQ) and a contact via WhatsApp app for assistance if necessary .

Figure 2 presents some interfaces as (a) user's personal data , (b) additional User Information such as blood type and whether the user is an organ donor and (c) allergy conditions such as allergy to egg or milk protein.

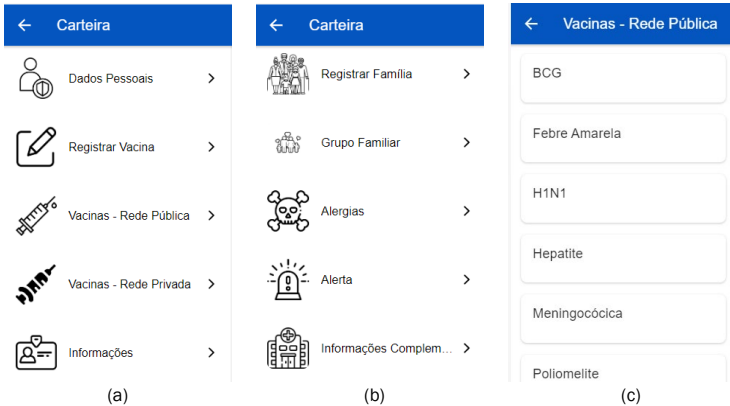
Figure 2. Digital Vaccine Card BR¹ interfaces: (a) User's personal data , (b) Additional User Information, (c) Allergy alerts.



Source: Author.

On these interfaces, figure 3, (a) there is a record of personal data (Dados Pessoais), vaccines received on the public network and vaccines received on the private network (Registrar Vacinas, Vacinas Rede Pública e Vacinas Rede Privada) , information about vaccines (Informações), (b) data on the family responsible - if necessary, minors, elderly, physically or mentally disabled (Registrar Família e Grupo Familiar), types of allergies presented by the user (Alergias), alerts about open vaccines, expired or upcoming vaccines, epidemiological alerts (Alertas). There is also the Health information function, where secure information bases are suggested (for example, sources from the Ministry of Health, Anvisa, World Health Organization and Fiocruz). In (c) there is a suggested link to check the vaccines available at each station (Vacinas- Rede Pública).

Figure 3. Digital Vaccine Card BR' interfaces: (a) Card's basic menu (b) Card's complementary menu and (c) Vaccines available.



Source: Author.

17.4.2 mHealth for Follow-Up of Brazilian Elderly People after Hospital Discharge

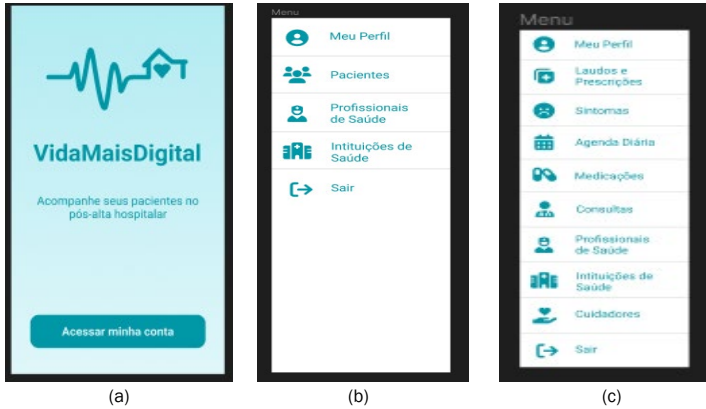
The model @MoreDigitalLife (in Portuguese, @VidaMaisDigital) aims to encompass the main functionalities necessary to help manage post-discharge monitoring of elderly patients. This mHealth solution was designed to facilitate communication among healthcare professionals or caregivers involved in patient care in the hospital and out-of-hospital settings. The application prototype was divided into two modules, one for healthcare professionals and the other for elderly patients and caregivers.

The application model was designed for the reality of the Discharge Management Office of Hospital Nossa Senhora da Conceição de Porto Alegre, considering the needs of health professionals who work in this service, taking into account the reality of elderly patients in this health institution. The application prototype was developed for mobile and web platforms, using the Figma platform.

Figure 4 presents the mHealth solution's presentation interface (a) and the menus: (b) presents the module menu intended for healthcare professionals, with an option for registering profiles of these professionals, registering patient profiles and profiles of Health Institutions related to care and (c) presents the module menu aimed at elderly patients, with the option of reports and prescriptions, patient symptoms, daily schedule,

medications, scheduled appointments, health professionals involved in the patient's care as well as caregivers and the Health Institutions that the elderly attend has contact.

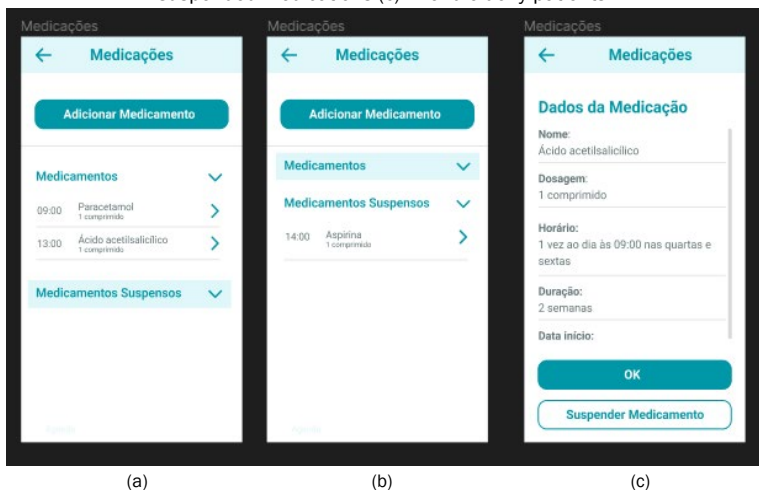
Figure 4. @MoreDigitalLife' interfaces: (a) main interface (b) menu for healthcare professionals options (c) menu elderly patients



Source: Author.

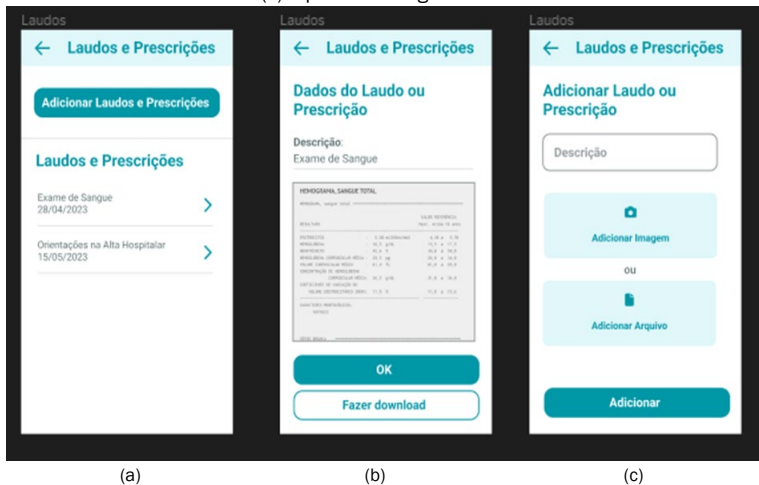
One of the fundamental issues for the correct treatment of elderly patients lies in the adequate use of the indicated medications. Figure 5 presents (a) the list of active medications indicated for elderly patients, in (b) the suspended medications that should no longer be administered to the elderly are observed, and in (c) the details can be seen of each medicine, indicating the daily quantity and time.

Figure 5. @MoreDigitalLife' interfaces: (a) list of active medications (b) List of suspended medications (c) menu elderly patients.



Source: Author.

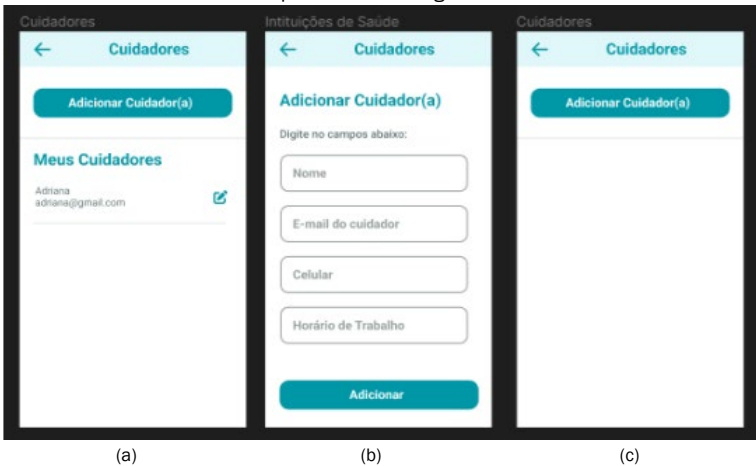
Figure 6. @MoreDigitalLife' interfaces: (a)list of reports and prescriptions (b) exam details (c) upload of images or exam files.



Source: Author.

In the mHealth solution, according to figure 6, it is possible to maintain the complete list of reports and prescriptions (a), making it possible for health professionals from health institutions who accompany the patient to have access to the details of the exams (b) and the elderly person or caregiver can upload the image of an exam or file with the exam report (c). Only professionals explicitly authorized by the Institution will have access to these reports and prescriptions.

Figure 7. @MoreDigitalLife' interfaces: (a)list of caregivers (b) date of caregiver (c) option to add caregivers.



Source: Author.

The control and list of caregivers for elderly patients is essential for the safety of the elderly and the trust of family members. Figure 7 presents the list of caregivers authorized to care for the elderly person (a), and data for each caregiver such as the time available to care for/accompany the elderly person (b) and the possibility of including and excluding caregivers from the list.

17.5 Discussion

Both mHealth solutions, in their specific contexts, were verified regarding the functional requirements defined in interviews with healthcare professionals, making it clear that the solutions managed to incorporate the defined functionalities. The solutions were also evaluated using evaluation

instruments focused on usability, ease of understanding and navigability. The convenience sample of health professionals and elderly people (those who agreed to participate after reading the Free and Informed Consent Form), presented positive feedback regarding the solutions and the content analysis of the responses presented by the sampled, reinforces the understanding that the solutions have the potential to evolve into a final product to meet the processes in the scenarios that allowed the conception of the mHealth solutions “BR Digital Vaccine Card” and “@MoreDigitalLife”.

17.6 Conclusion

Digital health has created opportunities and challenges for its implementation to effectively support healthcare professionals and patients, as well as the community at large. Vaccines have long proven the benefit they bring to the individual and the population collectively. Vaccination allows the general protection of individuals and requires monitoring from the first days of life and throughout the citizen's life. Aging and the emergence of different pathogens end up exposing the need for annual reinforcement of doses of some specific vaccines and monitoring the national vaccination plan ends up justifying the transition to digital solutions that allow governments to monitor the real vaccination coverage of the population.

As a limitation of the mHealth solutions detailed in this chapter, the challenge of obtaining a significant sample of healthcare professionals to evaluate both solutions, and of the post-hospital discharge elderly population to evaluate the mHealth @MoreDigitalLife solution stands out, which makes it impossible to generalization of the results obtained.

There are many future works based on the models and the prototyped mHealth solutions. The possibility of validating the solution with experimental use in healthcare processes in which it can be included can be highlighted. There is also scope for future work on information security and cybersecurity of solutions, as well as an in-depth study on the Return on Investment (ROI) for health institutions and municipal departments that could insert final products (final mHealth solutions and not prototypes) into their real processes.

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18 Monte Carlo Codes for Microdosimetric Simulations in Radiotherapy

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Abstract:

This chapter introduces the code based on the Monte Carlo (MC) method in the study of ionizing radiation applications in health sciences, particularly in Radiotherapy. Highlighting codes such as GEANT4-DNA, PARTRAC, TRAX-CHEM, gMicro-MC, PHITS, NASIC, TOPAS-nBio and IONLYS-IRT, the text explores their unique contributions to microdosimetric analysis. GEANT4-DNA enables detailed cellular-level simulations, TOPAS-nBio can accurately model radiation interactions at the cellular and subcellular levels in a user-friendly manner. PARTRAC specializes in modeling DNA damage, gMicro-MC utilizes GPU-based parallel computing for radiolysis simulations, NASIC focuses on nanodosimetric analysis, and IONLYS-IRT combines the modeling of subsequent chemical reactions. The chapter emphasizes the importance of these codes in advancing the safety and efficacy of innovative radiotherapeutic techniques, particularly those involving diverse particle beams.

Keywords: Monte Carlo; Microdosimetry; Radiotherapy.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 9. Industry, Innovation, and Infrastructure.

18.1 Introduction

Computational simulations are a widely employed tool within the scientific community to study the applications of ionizing radiation in health sciences. Due to the probabilistic nature of radiation-matter interactions, codes rooted in the Monte Carlo method (MC), an approach integrating randomness into extensive sampling, afford the capability to delineate the deposition of energy within a material [Kling et al 2014].

Within the field of Radiotherapy, the execution of MC simulations traditionally assumes a pivotal role in formulating planning systems, manufacturing dosimetric equipment, and overseeing quality in macroscopic contexts. Contemporary MC codes facilitate the construction of scenarios at cellular and subcellular tiers (ranging from organelles to DNA strand proteins), enabling the exploration of novel radiotherapeutic techniques via microdosimetric analysis (energy distribution) with consideration for the probability of chemical and biological effects on simulated structures. Despite certain variables appearing accountable for these outcomes, further investigation is warranted to elucidate the metabolic processes involved, ensuring the secure application of this innovative technique [Magrin et al 2023; Chatzipapas et al 2020].

Consequently, the objective of this study is to present some of the primary Monte Carlo codes for microdosimetric analysis employed in simulating radiotherapeutic scenarios. This contribution aims to facilitate the exploration and implementation of techniques utilizing different particle beams.

18.2 Microdosimetry

Computational simulations aimed at analyzing the dose in microscopic environments consider the heterogeneity of energy deposition in the medium, as well as the probabilities of biological damage caused in the simulated environment [Kellerer, 1975]. The information that fuels the possibilities of interaction with the medium in these codes comes from experimental measurements, which in turn have a limitation of ~1000 nm in diameter. Therefore, several Monte Carlo codes that aim to estimate the dose at micro or nanoscopic scales rely not only on the heterogeneity of energy deposition but also on experimental data and the cross-sections of particles representing the probabilities of interaction with matter.

18.3 Codes

In this section, the main Monte Carlo codes used for microdosimetric analysis will be briefly described. Table 1 presents the MC track-structure codes that are used in microdosimetric radiation effects studies. Energy ranges, particles, and target material and mainly references of the codes are indicated.

18.3.1 Geant4-DNA

Geant4-DNA serves as a low-energy extension of Geant4 (release 9.1), providing track-structure capabilities within the eV energy range [Incerti et al. 2010]. This extension facilitates the interaction-by-interaction transport of electrons, protons, hydrogen atoms, alphas, and certain ions in a liquid water medium. Currently, three sets of recommended alternative physics models are available, each corresponding to different cross sections for elastic and inelastic scattering [Bernal et al. 2015; Incerti et al. 2010]. The code has been extended to model the physical, the physicochemical, and the chemical stages of radiation interactions with liquid water.

Geometrical models down to the size of the DNA double helix are provided in dedicated examples [Bernal et al. 2015]. Within Geant4-DNA, the physicochemical stage encompasses the thermalization process of secondary electrons and electronic events taking place in ionized and excited water molecules, extending up to 1 picosecond (ps). The primary or secondary electrons that are produced during the physical stage get thermalized within 110 femtoseconds (fs) and then become solvated within about 250 fs [Shin et al. 2019].

The Geant4-DNA extension provides a complete set of models describing the step-by-step physical electromagnetic interactions of particles with liquid water. These models describe both the cross sections and the final states of the physical interactions, with a full description of the interaction products, considering the molecular structure of liquid water. Geant4-DNA can simulate the following physical interaction processes of the respective particle types with liquid water: 1. electrons: elastic scattering, electronic excitation, vibrational excitation, ionization and molecular attachment in the 7.4 eV - 1 MeV kinetic energy range; 2. protons and neutral hydrogen atoms: elastic scattering, electronic excitation, ionization, and electron capture or loss in the 100 eV - 100 MeV range; 3. helium atoms and their charge states: elastic scattering, electronic excitation, ionization and charge exchange in the 1 keV - 400 MeV range; 4.

other ions (Li, Be, B, C, N, O, Si, Fe): ionization only in the 0.5 MeV/u–106 MeV/u range [Bernal et al. 2015].

18.3.2 PARTRAC

PARTRAC is an established tool for Monte Carlo-based simulations of radiation track structures, damage induction in cellular DNA, and its repair [Friedland et al. 2011]. The code comprises a suite of interlinked modules programmed in FORTRAN (FORMula TRANslation). To model cellular DNA structures and estimate radiation effects on cellular DNA and their consequences, PARTRAC performs calculations of track structures produced by energetic ionizing particles within a region of interest. For this purpose, PARTRAC computes DNA damage in human cells by amalgamating simulated track structures within liquid water with a comprehensive "atom-by-atom" model of human DNA, considering the chromatin fiber structure and chromosomal territories. Due to its updates, PARTRAC is currently able to simulate photon interactions in a medium with arbitrary elemental composition, and tracks of electrons, protons, alpha particles, and heavy ions in liquid water. PARTRAC has been used for energy values below the relativistic threshold, where inelastic processes are well described by the non-relativistic Born first approximation (NR-PWBA) coupled to dielectric theory (DT) [Alloni et al. 2012].

In PARTRAC, dedicated modules describe interactions of ionizing particles with the medium, the production and reactions of reactive species, and score DNA damage determined by overlapping track structures with multi-scale chromatin models. The DNA repair module describes the repair of DNA double-strand breaks (DSB) via the non-homologous end-joining pathway. The code is also capable of simulating the yields and kinetics of radiation-induced chromosomal aberrations. Recent developments of the PARTRAC code include a model of hetero- vs euchromatin structures. Furthermore, the applicability of the code to low-energy ions has been extended to full stopping [Friedland et al. 2011].

Photon transport in PARTRAC is modeled using atomic cross sections taken from the Evaluated Photon Data Library, 1997 (EPDL97) [Cullen et al. 1997]. The considered phenomena include coherent scattering, photoelectric effect, Compton scattering, and pair production, as well as Auger electron emission and fluorescence photon emission. Cross-sections for liquid water or other biologically relevant materials are calculated from atomic cross-sections using the additivity rule and density scaling.

Presently, the code can calculate electron tracks from 10 eV up to 10 MeV, with due consideration given to the electron exchange and elastic scattering [Alloni et al. 2012]. The proton and alpha particle transport model of PARTRAC can operate for kinetic energies ranging from 1 keV to 1 GeV, considering excitations, ionizations, and the charge-changing processes of electron capture and loss. Elastic scattering is not considered [Friedland et al. 2011]. PARTRAC can also simulate segments of ion tracks heavier than helium from about 1 MeV/u up to 1 GeV/u (where u is the unified atomic mass unit), using velocity and charge scalability of proton cross-sections within the NR-PWBA and Bethe approximations [Friedland et al. 2011].

18.3.3 TRAX-CHEM

This is an extension of the TRAX code, which, in turn, was one of the first to model track structure for electrons and heavy ions, including their interaction with the material medium. Additionally, it was among the pioneers in addressing nanoparticle sensitization for proton beams. The TRAX-CHEM operates with a step-by-step approach, differing from the technique that analyzes the so-called independent reaction time (IRT), considering the physical, pre-chemical, and chemical stages by a temporal scale of ionizing radiation interaction with matter [Kramer et al 1994].

In the physical stage ($<10^{-15}$ s), in the case of the target being composed of water, the simulated ionization processes consider the cross-section of five distinct layers and eight excitation states of the molecule, each defined by a specific chemical reaction according to the TRAX code. In the pre-chemical stage ($\sim 10^{-15}$ s to 10^{-12} s), the products formed in the previous stage undergo dissociation, i.e., the spatial distribution of all radicals resulting from the passage of radiation in the medium, ensuring the exact position of each at the end of this stage. Thermalization is simulated in a single step, considering the dissociated fragments and their ability to interact with their neighbors. For this, the excess energy from reactions is computed by analyzing a diffusion coefficient, the temperature of the medium, and the displacement time of the radicals. Finally, in the chemical stage (10^{-12} s to 10^{-6} s), the products from the previous stage can be spatially tracked at each simulated time step. In this stage, the following are simulated: (1) radical diffusion, modeled as a jump in a random direction with its size selected within a 3D Gaussian distribution, and (2) the chemical reactions of each formed product, assessed according to a parameter called the reaction radius, defined according to the Smoluchowski theory

that deals with Brownian motion.

Among its applications, this extension allows for the study of the temporal evolution of chemical species (G-values), as well as the recombination between radicals formed after the deposition of radiation energy in the medium. Additionally, the behavior of Linear Energy Transfer (LET) can be analyzed concerning different G-values for each material, thus being crucial to aid in understanding biological damage in systems, especially in complex oxygenated scenarios [Boscolo et al 2018].

Table 1. Key parameters associated with Monte Carlo track structure codes.

Code	Energy Range	Particles	Target Materials	References
TRACX-CHEM	1 eV - several MeV	e-, e+, p, ions	water (vapor phase)	[Boscolo et al 2018]
TOPAS nBio	e- (thermalization -1MeV); p, H (100 eV -100 MeV); α (1 keV - 400 MeV); ions (0.5 MeV/u - 10^6 MeV/u**)	e-, p, H, α , ions	liquid water, DNA, Gold	[Schuemann et al 2019]
gMicro MC	4.3 eV - ?	e-, p, heavy ions	liquid water, DNA	[Lai et al., 2020]
PHITS	n, μ (0.01 meV - 1 TeV) p, γ (1 keV - 1 TeV) e (1 meV - 1 TeV) nucleus (1 keV - 1 TeV/n*)	all particles	liquid water, DNA	[Sato et al., 2023]
GEANT4-DNA	e- (thermalization -1MeV); p, H (100 eV -100 MeV); α (1 keV - 400 MeV); ions (0.5 MeV/u - 10^6 MeV/u**)	e-, p, H, α , ions	liquid water, DNA, Gold	[Incerti et al. 2010; Bernal et al. 2015]
NASIC	thermalization - 1 MeV e-	e-	liquid water	[Li et al. 2015]
IONLYS IRT	e-, p (0.2 eV - 150 keV); ions (0.1 MeV - 300 MeV)	e-, p, ions	liquid water	[Cobut et al. 1998]
PARTRAC	(1 eV - 10 MeV) e-, (1 keV - 1 GeV) p, H, α , (1 MeV/u - 1 GeV/u) ions	e-, e+, p, H, α , ions	liquid water, DNA	[Friedland et al. 2003]

*TeV per nucleon

** u is the unified atomic mass unit

18.3.4 TOPAS-nBio

The TOPAS-nBio is presented as an open-source set of classes that extends the main parameter system of TOPAS to configure specialized simulations at the cellular and subcellular levels for modeling radiobiological experiments. Based on the Geant4-DNA toolkit, as well as

the foundational Geant4 framework of TOPAS, it serves as a tool capable of bridging Monte Carlo simulations for medical physicists inexperienced in C++ programming [Perl et al., 2012; Schuemann et al., 2018].

Regarding geometries, the Geant4 toolkit offers users basic geometric volumes such as spheres, boxes, or ellipsoids, which are also available in TOPAS-nBio, and in some cases, as compositions of these, providing an extensive catalog of geometries specialized in radiobiology. To facilitate the use of these structures, a user interface has also been developed [McNamara et al. 2018].

For Monte Carlo Track-Structure simulations, the transport of charged particles and their interactions occurs step by step, using physical processes and associated models configured according to Geant4-DNA. This allows the inclusion of particle interactions ranging from very low energy to vibrational energies, without using condensed histories and propagating radiolysis products, as mentioned earlier in this study and fundamentally by Incerti et al. (2018).

18.3.5 gMicro-MC

Developed by the Physics Research & Techniques Radiation Medicine at the University of Texas at Arlington, gMicro MC presents itself as a highly efficient open-source tool that utilizes a parallel computing technique based on Graphic Processing Units (GPUs). Like other proposals, this software performs its metrics based on the radiolysis process, considering the interaction of charged particles (electrons and heavy ions) [Lai et al. 2021] with water molecules and computing the probabilities of DNA damage through the energy deposition spectrum.

The algorithm was designed to simulate the ionization process in three stages. Initially, the physical stage ($<10^{-15}$ s) evaluates the energy transport of electrons, the formation of secondary particles, and the ability to interact with water molecules based on the cutoff energy and cross-section of each layer of molecules. The model incorporates ionization, excitation, elastic collision, and electronic dissociation processes. In the physical-chemical stage ($\sim 10^{-15}$ s to 10^{-12} s), like PARTRAC, the algorithm determines which radicals will be formed and where, through the ionization and excitation pathways of water molecules, as well as the thermalization processes of fragments generated by hot dissociations and electronic sub excitation. Finally, the chemical stage ($\sim 10^{-12}$ s to 10^{-6} s), modeled by the Brownian motion diffusion of various individually formed radicals (e^{-aq} , $\cdot OH$, $H\cdot$, H_3O^+ ,

H², OH, and H₂O₂), evaluates their trajectory and the possibilities of recombination of the radicals themselves, based on the distance between reactants and the radius of each reaction, using both PARTRAC and GEANT4-DNA [Tsai et al., 2020]. As for the geometry library, gMicro MC provides a range from nucleotide pairs (with cylinders of 1 nm in diameter and 0.34 nm in height) to double-helix DNA, nucleosomes, chromatin fiber loops, chromatin fiber units, and even cell nuclei of lymphocytes with a diameter of 11 μm. By overlaying spatial information from chemical reactions and the initially configured geometry, the DNA damage is ultimately computed. The code eliminates duplicate sites and considers the highest probabilities of occurrence for both single-strand breaks (SSB) and double-strand breaks (DSB) [Lai et al., 2020].

18.3.6 PHITS

The Particle and Heavy Ion Transport Code System (PHITS) is a multipurpose system based on the Monte Carlo method, which considers virtually all types of particles. Since 2019, it has been freely distributed by the Japan Atomic Energy Agency (JAEA) upon request and under usage control guidance [Iwase et al, 2002]. Recent data indicate over 4,000 registered users in 68 countries. This platform is compatible with Windows, Mac, Linux, and Unix operating systems according to the desired version for installation. The latest versions have significant computational power, reducing simulation time by a third (from 18.4 s to 6.2 s) in the case of shielding calculations [Sato et al., 2023].

This project was developed through a partnership between development centers in Europe and Japan. It is written in FORTRAN language, derived from a combination of validated codes such as the Nucleon-Meson Transport Code (NMTC) and Jet AA Microscopic Transport Model (JAM), enabling the simulation of particles with cascades of nuclear reactions for energies up to 200 GeV [Niita, 2001]. The system was developed in conjunction with two other codes: Heavy Ion Code and ISABEL, designed to analyze interactions of heavy ions with energies greater than 50 MeV per nucleon. There are also a variety of models and libraries available capable of handling problems ranging from less complex to nuclear fission situations, phonon resonance, and shielding calculations with neutron production.

There is a specific package (RT-PHITS) capable of working with images in the DICOM format (Digital Imaging and Communications in Medicine).

This package has two modules (CT2PHITS, PET2PHITS) responsible for converting CT (Computed Tomography) and PET/SPECT (Positron Emission Tomography/Single Photon Emission Tomography) images into a representative geometry of the human body capable of simulating dose deposition in organs (Figure 2). Additionally, the Plan2PHITS module features a Graphical User Interface (GUI) that allows users to change beam parameters and simulate a radiotherapeutic treatment. The PHITS2DICOM module converts energy deposition values into doses with a 3D spatial distribution in the images previously loaded into the system. Consequently, it is possible to estimate DNA damage by calculating single and double-strand breaks (SSB, DSB) using photon, proton, electron, and even ion beams [Sato et al., 2023].

18.3.7 NASIC

NASIC (NANodosimetry Monte Carlo Simulation Code) is a Monte Carlo simulation code for nanodosimetric analysis [Li et al. 2015] that was developed by Tsinghua University (Beijing, China), and comprises physical, pre-chemical, chemical, geometric, DNA damage, DNA damage repair, and cell death modules. In its physical module, the transportation processes of low-energy electrons in the liquid water, including the secondary electrons, are simulated event by event. The code includes inelastic cross-sections of low energy electrons in liquid water from 8 eV to 10 keV, considering ionization and excitation processes [Li et al. 2020]. The elastic cross sections and the vibrational excitation cross sections are directly taken from Geant4-DNA. The inelastic cross sections are calculated based on the dielectric function method of Emfietzoglou's optical-data treatments.

In the pre-chemical module, the ionized and excited water molecules undergo certain dissociation processes and produce some radiolytic chemical species. The chemical stage also employs a step-by-step approach and mainly covers the time interval from 1 ps to 1 ns, during which the chemical species and the molecular products diffuse and react. The geometric module has two types of DNA target models: the volume model and a much more detailed atomic model. The DNA damage module is related to the DNA model and currently is only available for the volume model. There are three parameters needed in this module: the threshold energy for inducing one strand break (ESSB), the probability for -OH radicals to cause one strand break (POH) and the scavenging capacity parameter (denoted as C_{sca}) for calculating the probability of the -OH radicals

scavenging by the scavengers [Li et al. 2015].

To calculate the cross sections, the low-energy correction function proposed by Paretzke is adopted for perturbation correction. Additionally, the Born-Møller cross-section method [Nikjoo et al. 2012] is used for the electron exchange effect correction. The remaining cross-sections related to electron interactions are directly sourced from Geant4-DNA, while those for photons and gold are exclusively drawn from Geant4. Consequently, the physics module of NASIC is fundamentally rooted in Geant4 and Geant4-DNA, except for the electron ionization/excitation cross-section in liquid water. For photons, NASIC replicates phenomena such as Compton scattering, photoelectric absorption, gamma conversion, and Rayleigh scattering. Concerning electrons, the simulated processes within liquid water involve elastic scattering, ionization, excitation, attachment, and vibrational processes. In the case of gold, the code encompasses multiple scattering, ionization, and bremsstrahlung. In liquid water, NASIC employs the condensed history electron transport method, where the cumulative effects of multiple electron collisions are approximated within a single 'step' of path length, determined by the user. However, when dealing with gold, the track structure method is applied, aiming to model the trajectory of charged particles as they traverse a medium, considering the distinct behavior of each particle [Li et al. 2020].

18.3.8 IONLYS IRT

The IONLYS-IRT code [Cobut et al. 1998] was developed by a group from Université de Sherbrooke. This Monte Carlo code first models, in a 3D geometric environment, the initial, highly non-homogeneous radiation track structure ("IONLYS" program), followed by the ensuing diffusion and chemical reactions of the various radical and molecular products formed by radiolysis ("IRT" program). The IONLYS program is used to model the early physical and physicochemical stages of the radiation action up to ~1 ps in track development. It accurately models, event by event, all the basic physical interactions (energy deposition) and the subsequent conversion of the locally generated physical products into the different initial radical and molecular products of the radiolysis [Sepulveda et al. 2018].

The complex spatial distribution of the reactants at the end of the physicochemical stage, provided as an output of the IONLYS program, is subsequently used as a starting point for the ensuing non-homogeneous chemical stage. The IRT program takes charge of the simulation's third

stage, employing the "independent reaction times" (IRT) method - a stochastic simulation technique capable of simulating reaction times without the need to trace the trajectories of diffusing species [Sepulveda et al. 2018]. This IRT program can also be used efficiently to describe the reactions that occur at longer times when the radiolytic products are homogeneously distributed throughout the bulk solution [Sepulveda et al. 2018].

The IONLYS simulation program encompasses the early physical and physicochemical stages of radiation action up to $\sim 10^{-12}$ s. It models, event by event, all fundamental physical interactions (energy deposition) and the subsequent attainment of thermal equilibrium in the system. Following the completion of the physical stage, it further simulates the conversion of locally generated physical products into diverse initial radical and molecular products of radiolysis. These products are distributed within a highly non-homogeneous track structure [Meesat et al. 2012].

18.4 Conclusion

The track structure and irradiation target properties are the main physical entities related to radiation-induced damage. The processes of secondary electron production and radical interactions are inherently stochastic and, therefore, they can be studied through a statistical approach with Monte Carlo codes. The Monte Carlo codes presented in this chapter exemplify this advancement in simulations by enabling an in-depth radiobiological study.

In summary, Geant4-DNA is capable of simulating the physical interaction processes of electrons, protons and neutral hydrogen atoms, helium atoms and their charge states and a few ions - down to \sim eV scale - with liquid water. The code allows for the analysis of radiation effects at microscopic scales, contributing to a deeper understanding of radiobiological impacts at the subcellular level. PARTRAC is capable of modeling cellular DNA structures, estimating radiation effects on cellular DNA and simulating the yields and kinetics of radiation-induced chromosomal aberrations. The TRAX-CHEM presents a step-by-step approach, being one of the first to allow tracking the production of radiolytic products responsible for damage to DNA strands, serving as a foundation for later codes. The TOPAS-nBio utilizes physical and chemical models from well-established codes in the scientific community but with a more user-friendly interface. This allows greater accessibility for beginners in the study

of simulations with ionizing radiation. The gMicro-MC is the most recent tool among those presented, developed with GPU-based computational techniques, significantly reducing the machine time required for microdosimetric computational simulations. As for PHITS, it is a system with a comprehensive set of tools and a graphical interface, available for free. This enables user interaction for constructing complex scenarios on various scales and with a wide range of energies. Through NASIC, the influence of inelastic cross sections and vibrational excitation reaction on the parameters of the modules and the DNA strand breaks can be studied. The IONLYS-IRT code has been used to simulate in complete detail the radiolysis of the studied Fricke/cystamine solutions. Beyond that, IONLYS-IRT models all the basic physical interactions and the subsequent establishment of thermal equilibrium in the system, which are distributed in a highly non-homogeneous track structure.

Finally, research involving microdosimetric simulations based on the Monte Carlo method is a crucial step in validating new techniques using ionizing radiation, as it optimizes and guides *in vitro* and *in vivo* studies, leading to more efficient development of experimental scenarios and theories.

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19 Artificial Intelligence for Medical Diagnosis: Employing an Explainable Convolutional Neural Network Approach in the Classification of Brain Tumors

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Abstract:

This chapter discusses developing and applying a Convolutional Neural Network model for classifying brain tumors in MRI scans. The focus is on overcoming the limitations of manual and subjective analysis prevalent in traditional methods by offering an automated solution. The model was trained using a comprehensive dataset of MRI images and subsequently evaluated using a distinct, independent dataset. In validation tests, the model achieved an accuracy rate of 99%, which compares favorably to the performance of existing methods. This chapter further explores the implications of these results for the model's utility in medical imaging diagnostics while also considering the role of Explainable AI techniques in elucidating the model's decision-making processes.

Keywords: Brain Tumor, Deep Learning, Convolutional Neural Network.

Sustainable Development Goals (SDG): 3. Good Health and Well-being.

19.1 Introduction

Explainable Artificial Intelligence (XAI) is a crucial development in artificial intelligence (AI) to make AI systems' decision-making processes transparent and understandable. In critical applications like healthcare, XAI ensures that AI-based decisions are accurate and comprehensible to practitioners and patients. This transparency is essential for building trust and adhering to ethical standards by providing insights into how AI models derive their conclusions.

In this study, we focused on applying XAI to classify brain tumors using Convolutional Neural Networks (CNNs). We developed a CNN model capable of accurately classifying brain tumors from MRI scans and elucidating its decision-making process, which is particularly important in the medical field for building trust in AI-generated diagnoses.

The World Health Organization (WHO) defines a brain tumor as an intracranial growth of abnormal cells, whether primary or secondary, with the potential for uncontrolled growth and impact on adjacent brain tissue. Brain tumors can be malignant, characterized by rapid, disorganized cell growth, or benign, featuring slower, more organized growth. While benign tumors are generally less life-threatening, they can still pose significant health risks if they grow large or impact crucial brain areas (Louis et al. 2016).

Diagnosis of brain tumors typically involves advanced brain imaging techniques, particularly MRI, known for its high resolution and capability to differentiate between various brain tissues (Louis et al. 2021). These advanced techniques, such as diffusion-weighted and perfusion imaging, have significantly enhanced the accuracy of diagnoses and informed treatment planning (Nandu et al. 2018). Complementing this, the WHO employs a four-tiered grading system based on histopathological criteria, immunohistochemical data, and the degree of malignancy for classifying primary tumors (Perkins and Gerald 2016). This classification determines treatment intensity according to the tumor's grade.

However, accurate classification can be challenging due to the tumors' diverse appearances and characteristics. This complexity necessitates skilled professionals for accurate diagnosis and treatment planning (Wadhwa et al. 2019). Limited access to such professionals and advanced diagnostic tools can lead to misdiagnosis or inadequate care in less developed areas.

Our study presents a Computer-Aided Diagnosis (CAD) system to address these challenges, based on CNNs and enriched with XAI methods. This system, trained on an extensive dataset of MRI images, is designed to effectively classify brain tumors while providing interpretable insights into its analytical processes. We structured this chapter into four sections: an introduction to CNNs and XAI, the methodology for developing the CNN model with XAI integration, the results from our network training, and a discussion on the implications of our findings, which includes an examination of the role of XAI in improving the trust and effectiveness of medical diagnostic processes and considerations for future research in this area.

19.1.1 Previous Results

In a preceding study, we achieved an impressive accuracy rate of 99% in our model for brain tumor classification (Felipe et al. 2023). While this marked success underscored the proficiency of our model in accurately discerning different tumor types from MRI data, it is essential to acknowledge a significant limitation in our approach. Regrettably, our prior study did not delve sufficiently into XAI concepts. Recognizing the increasing importance of understanding the decision-making processes of artificial intelligence models, we acknowledge this gap in our previous research and aim to address it comprehensively in the current study.

In our current investigation, not only do we maintain a robust focus on accuracy, but we also emphasize the interpretability of our model. To enhance transparency, we display the probabilities associated with each class, providing insights into the confidence levels of our model's predictions. Moreover, we extend our efforts beyond the limitations of our previous study by implementing advanced explainability techniques. Specifically, we employ Gradient-weighted Class Activation Mapping (Grad-CAM) for a single layer and every convolutional layer within our model architecture. This multi-layered approach to Grad-CAM visualization aims to provide a more detailed and nuanced understanding of the salient features influencing the model's decision-making at various hierarchical levels. By combining high accuracy, probability display, and comprehensive Grad-CAM visualization across all convolutional layers, we strive to establish a model that excels in predictive performance and elucidates the reasoning behind its classifications.

19.2 Materials and Methods

19.2.1 Development Environment and Technologies

For this project, we chose Google Colab as the primary development environment. We utilized prominent libraries such as TensorFlow, scikit-learn, and Keras to support the development of our model. These libraries offered essential resources and methods for enhancing model performance and ensuring precise predictions. We obtained the dataset for our study from Kaggle, which provided a broad and varied collection of images suitable for training and testing the model. Key factors in selecting the dataset included its suitability for classification and evaluation and the volume of images it contained.

19.2.2 Data Description and Pre-Processing

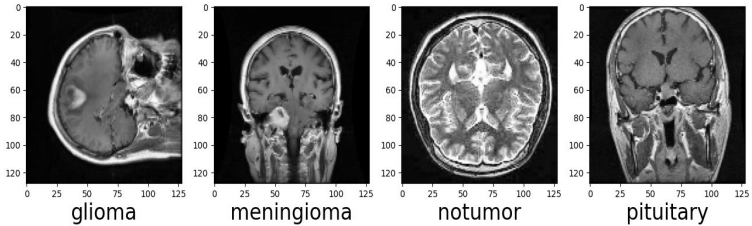
This research utilized a dataset from the "Brain Tumor MRI Dataset," which included 7023 images divided into two main categories: a testing set with 1311 images and a training set comprising 5712 images. Within these categories, images were further organized into four subfolders labeled glioma, meningioma, notumor, and pituitary, reflecting the type of tumor or absence thereof.

During the research, we discovered that some images in the Glioma subfolder needed to be correctly labeled. These images were replaced with correctly labeled ones from the "Figshare Brain Tumor Classification" dataset in order to maintain the dataset's accuracy. This correction was crucial to ensure the validity and reliability of the study's results.

After these adjustments, the training set's composition was as follows: glioma (1140 images, 20.61%), meningioma (1339 images, 24.21%), notumor (1595 images, 28.84%), and pituitary (1457 images, 26.34%). This distribution provided a balanced representation of different tumor types for the model's training.

The final dataset for the study consisted of 5531 training images and 1297 test images. Additionally, 20% of the training images were randomly selected to form a validation set. All images were resized to a uniform resolution of 128x128 pixels to ensure consistency and computational efficiency. Pixel values in the images were normalized by scaling them to a range of 0 to 1, dividing each value by 255. This normalization was crucial for avoiding numerical instability and aiding the model's convergence. Figure 1 in the study showcases representative images from each class, including glioma, meningioma, notumor, and pituitary.

Figure 1. Examples of images referring to each possible class.



19.2.3 Addressing Data Balancing and Leakage

During this study's preliminary data analysis phase, we identified a disparity in the distribution of images among the different classes, which necessitated measures for data balancing. For this purpose, we assigned specific weights to each of the four classes during the training phase. We distributed the weights: glioma class received a weight of 1.21, meningioma class 1.03, notumor class 0.86, and pituitary class 0.94.

The data fragments in all validation folds were shuffled prior to training to ensure the model's ability to generalize and avoid skewed results. This shuffling process is essential for encouraging the model to learn in a more generalized and robust manner, thereby improving its overall performance in unfamiliar scenarios. Additionally, it reduces the likelihood of the model memorizing specific training data patterns.

We first divided the dataset into training and validation sets before applying normalization to avoid data leakage, which can compromise the model's validity. Furthermore, we utilized K-Fold Cross-Validation as a protective measure. This technique is critical in ensuring that the training set is not inadvertently influenced by the validation set, particularly during the normalization stage, thus preserving the integrity and reliability of the model's evaluation.

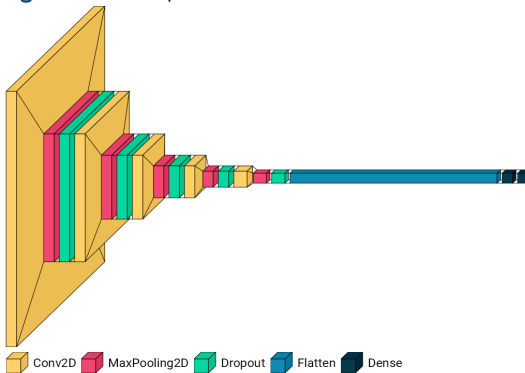
19.2.4 Model Architecture and Settings

The constructed model features a series of five convolutional blocks, each designed to process images through multiple layers and handle various multidimensional data types. These convolutional layers utilize learnable filters that apply to the input data, enabling the extraction of essential features for further processing. The architecture of the model, including these layers, is depicted in Figure 2.

Each convolutional block includes max-pooling layers to reduce the dimensionality of the input data and dropout layers to mitigate overfitting by randomly omitting neurons during the training process. The convolutional layers are configured with 3x3 kernels using the ReLU activation function. The configuration of filters and dropout rates across the five layers is as follows: the first layer has 16 filters with a 20% dropout rate; the second has 32 filters with a 25% dropout rate; the third consists of 64 filters with a 30% dropout rate; the fourth contains 128 filters with a 35% dropout rate; and the fifth layer has 256 filters with a 40% dropout rate. This structure allows the model to capture a wide range of features effectively.

The model employs fully connected layers for the classification task. The first of these layers contains 32 neurons, using ReLU activation and L2 regularization. The subsequent layer, consisting of four neurons, employs softmax activation for multi-class classification and incorporates L2 regularization.

Figure 2. Visual representation of the model's architecture.



We used the Adam optimization function to efficiently update the weights for the optimization process. The loss function selected for the model is sparse categorical cross-entropy, which aids in minimizing the discrepancy between predicted and actual labels during training. Accuracy is the primary metric employed to visualize the model's performance over time comprehensively.

19.2.5 Training

During this study's preliminary data analysis phase, we identified a disparity in the distribution of images among the different classes, which necessitated measures for data balancing. For this purpose, we assigned specific weights to each of the four classes during the training phase. We distributed the weights: glioma class received a weight of 1.21, meningioma class 1.03, notumor class 0.86, and pituitary class 0.94.

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19.3 Results

The neural network's performance in this study was notable, with an overall accuracy surpassing 99% on the test set throughout the validation phases. Breaking down the accuracy by individual classes, the network achieved 100% for glioma, 99% for meningioma, 99% for notumor, and 98% for pituitary. This high accuracy across different classes reflects the model's prediction precision.

In addition to accuracy, we also evaluated the recall rate of the model, which focuses on correctly identifying true positive cases. The recall rates were 100% for glioma, 97% for meningioma, 99% for notumor, and 100% for pituitary. These results underscore the model's capability to detect true positive cases effectively in each class, with a particularly strong performance in identifying no tumor and pituitary cases.

Table 1 presents critical metrics, including precision, recall, F1 score, and accuracy. Precision is the measure of true positive predictions out of all positive predictions made by the model, while recall assesses the proportion of true positives detected out of all actual positives. The F1

score, a harmonic mean of precision and recall, is employed to gauge the model's overall performance. Accuracy, however, calculates the total percentage of correct predictions made by the model across all classes.

Table 1.1. Classification report categorized by class.

	precision	recall	f1-score	support
glioma	1.00	1.00	1.00	286
meningioma	0.99	0.97	0.98	306
notumor	0.99	0.99	0.99	405
pituitary	0.98	1.00	0.99	300
accuracy	N/A	N/A	0.99	1297
macro avg	0.99	0.99	0.99	1297
weighted avg	0.99	0.99	0.99	1297

The visual aids included in this study offer an in-depth evaluation of the model's performance. Figure 3, in particular, depicts the training and validation loss over 100 epochs, shedding light on the model's ability to generalize to new, unseen data. This extensive epoch range allows for a detailed analysis of trends over time. Moreover, the depicted results incorporate data from five different cross-validation folds to comprehensively evaluate the model's performance.

Figure 4 focuses on accuracy, a crucial metric in machine learning that measures how often the model makes correct predictions. This figure complements the insights gained from Figure 3 by illustrating how the model's accuracy evolves throughout training and validation. It presents training and validation accuracy metrics over the same 100 epochs, spanning the five cross-validation folds. The combined analysis of Figures 3 and 4 offers a comprehensive view of the model's performance, particularly highlighting its proficiency in generalizing to new datasets.

Figure 3. Loss graph of the 5 cross validation folds.

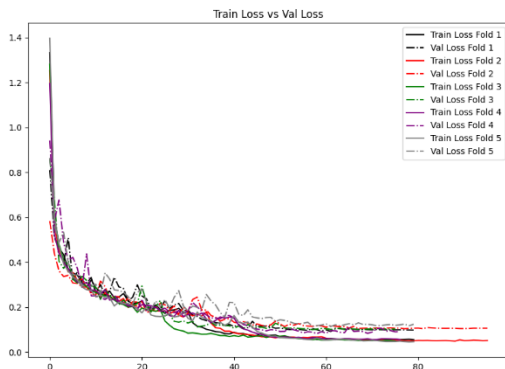
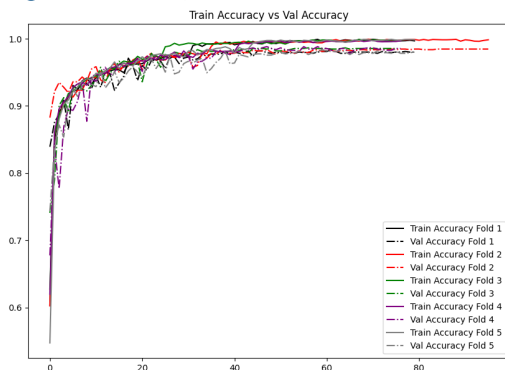


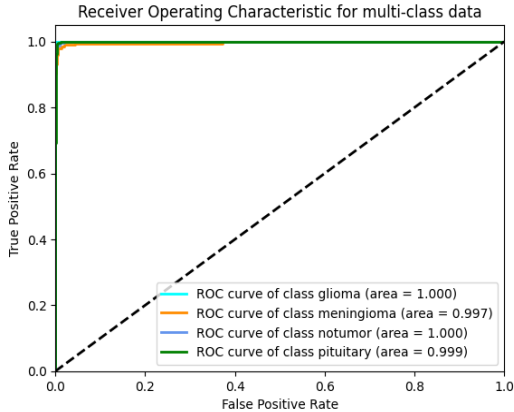
Figure 4. Accuracy graph of the 5 cross validation folds.



The Receiver Operating Characteristic (ROC) curve is a critical tool for assessing the efficacy of binary classification. This curve illustrates the trade-off between the true positive rate (sensitivity) and the false positive rate ($1 - \text{specificity}$) at different thresholds. The Area Under the ROC Curve (AUC-ROC) concisely summarizes the model's overall classification performance, where a higher AUC-ROC value signifies better classification ability. In our study, the ROC curve, as shown in Figure 5, approaches the upper left corner, indicating a favorable balance between true positive and false positive rates.

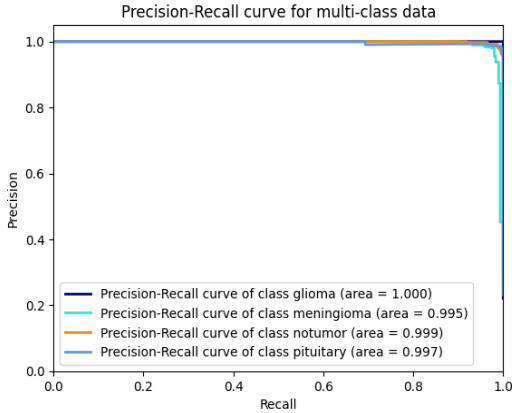
Deep Learning models, including CNNs, are often critiqued for their lack of transparency, a significant issue in fields like medical imaging where understanding the decision-making process is crucial. In this context, our study utilizes a CNN for brain tumor classification, consciously addressing the challenges of interpretability inherent in such models.

Figure 5. ROC curve generated from the trained model.



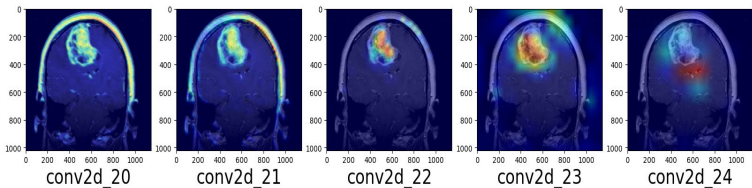
In order to provide a comprehensive assessment of the performance of our CNN model, we prepared a precision-recall analysis. This analysis is essential in evaluating the trade-off between the precision (the proportion of true positive results among all positive predictions) and the recall (the ability of the model to identify all relevant instances) of the model. Precision-recall curves are particularly useful in scenarios with an imbalance in the representation of classes, as is often the case in medical imaging datasets. By plotting precision against recall for different thresholds, we can visualize the balance between these two metrics at various levels of classification threshold. This analysis not only aids in understanding the model's capability to distinguish between classes but also provides insights into how we manage the balance between false positives and false negatives. Such an evaluation is crucial in medical applications, where the cost of false negatives might be significantly high. The results of this precision-recall analysis for our CNN model are detailed in Figure 6, offering an integral view of the model's performance in classifying brain tumors.

Figure 6. Precision-Recall curve generated from the trained model.



To enhance the transparency of the artificial intelligence model, we incorporated Grad-CAM, an advanced technique designed to improve the model's interpretability. Grad-CAM aids in visualizing the areas within input images, significantly influencing the outcomes at various convolutional layers. This method allows for a detailed insight into the model's decision-making process, which is particularly beneficial for complex operations like image classification. Doing so addresses the common issue of opacity in AI models. In Figure 7 of our study, we presented heatmaps for each convolutional layer, illustrating the specific regions in the images that were pivotal in the model's analysis.

Figure 7. GRAD-CAM heatmaps generated from Meningioma images of the "Brain Tumor MRI Dataset" (15) test set.



In addition to the Grad-CAM visualization, our study incorporated a probability display for each class to provide a thorough interpretation of the model's predictions, as illustrated in Figure 8. Expanding the Grad-CAM

approach to include heatmap visualizations for each convolutional layer enhances model interpretability at a broad level and in terms of the nuanced, hierarchical features learned by the model. By integrating the Grad-CAM technique with the visualization of class probabilities across convolutional layers, we established a dual approach that significantly contributes to developing a more interpretable AI framework, particularly vital in fields where transparency and dependability are paramount.

Figure 8. Probability display for each class, generated from Meningioma images of the "Brain Tumor MRI Dataset" (15) test set.

```
1/1 [=====] - 0s 126ms/step
Probability of 'glioma': 0.00%
Probability of 'meningioma': 60.43%
Probability of 'notumor': 0.27%
Probability of 'pituitary': 39.30%
```

19.4 Conclusion

In this chapter, we have successfully illustrated the profound impact of a CNN model in brain tumor classification using MRI scans, achieving a notable accuracy rate of 99%, representing a substantial step forward, surpassing traditional methods with an automated, more reliable approach.

It is, however, essential to recognize the limitations and potential avenues for improvement within this model. Broadening the dataset to encompass various images could substantiate the model's efficacy. A critical examination of errors affecting precision and recall is crucial for ongoing enhancements. Integrating strategies like Data Augmentation may also enhance the model's generalizability.

Additionally, this research underscores the importance of XAI in this context. XAI techniques are pivotal in making the model's decision-making processes transparent and understandable, which is vital for gaining trust and acceptance in clinical applications.

In conclusion, the findings of this study highlight the immense promise of deep learning, particularly CNNs, in refining brain tumor classification. They also emphasize the significance of XAI in the medical field, supporting the development of more accurate and efficient diagnostic tools. Researchers should actively continue to explore and refine deep learning models in medical imaging, fully harnessing their capabilities and clearly understanding their implications to maximize their impact in clinical settings.

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20 Convergence of Knowledge: Legacy of a Pioneering Interdisciplinary Graduate Program at the Federal University of Health Sciences of Porto Alegre

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Mellina da Silva Terres
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Rafaela Soares Rech

Abstract:

The Coordination of Superior Level Staff Improvement (CAPES) is a foundation linked to the Brazilian Ministry of Education (MEC), dedicated to expanding and consolidating stricto sensu graduate studies in Brazil. This chapter summarizes the significance and contributions of interdisciplinary knowledge areas to research and the training of Brazilian researchers, drawing on data from a CAPES report. It also highlights the legacy of the Graduate Program in Information Technologies and Health Management (PPGTIGSaúde) at the Federal University of Health Sciences of Porto Alegre (UFCSPA), a pioneering program that embodies the interdisciplinary knowledge approach. Lastly, the chapter will discuss the challenges and opportunities associated with developing an academic graduate program in interdisciplinary studies within the context of PPGTIGSaúde.

Keywords: interdisciplinarity; graduate program; legacy.

Sustainable Development Goals (SDG): 3. Good Health and Well-being; 04. Quality Education; 10. Reducing inequalities.

20.1 Introduction

Since its establishment in 1951, the Coordination of Superior Level Staff Improvement (CAPES)⁴ has played a crucial role in coordinating and promoting postgraduate programs across Brazil. Initially, the focus was primarily on disciplinary programs, reflecting the academic structure of the time. However, the need for more integrated and collaborative approaches became increasingly evident. It was not until 1999 that CAPES formally acknowledged the significance of interdisciplinarity by creating knowledge area 45. This area serves as a pivotal space for CAPES to engage with the national postgraduate system, characterized by its transdisciplinary nature. It aims to transcend disciplinary boundaries, articulating, transforming, and generating concepts, theories, and methods that bridge different realms of reality, logics, and forms of knowledge production, distinguishing itself from traditional disciplinary frameworks (CAPES, 2014).

In an era where challenges have become so complex that individual fields of knowledge often reach their limits—even with the expertise of skilled researchers—the potential for interdisciplinary integration becomes clear. Issues confronting future health researchers, such as population aging, increased longevity, pandemics, climate change, rapid technological advancements, and the rising importance of Digital Health, underscore the significance of CAPES interdisciplinary knowledge area. LIMA (2022) emphasizes the challenges of interdisciplinarity in the health sector during the COVID-19 pandemic, notably highlighting the overwhelming spread of misinformation that has affected the population.

In response to the challenge of preparing researchers for a demanding future in a relatively new area of knowledge, the Graduate Program in Information Technologies and Health Management (PPGTIGSaúde) at UFCSPA (UFCSPA, 2024) was established in 2018 as an academic master's program within CAPES interdisciplinary knowledge area.

In this chapter, we summarize the significance and contributions of the interdisciplinary knowledge area to research and the training of Brazilian researchers, drawing on data from a CAPES report. We will also explore the legacy of the PPGTIGSaúde, a pioneering program that embodies the interdisciplinary approach. Finally, we will discuss the challenges and opportunities involved in developing an academic graduate program in the interdisciplinary area within the context of PPGTIGSaúde.

⁴ <https://www2.camara.leg.br/atividade-legislativa/comissoes/comissoes-mistas/cpcms/siglas/siglar2/c/CAPES.html>

20.2 Interdisciplinary Area

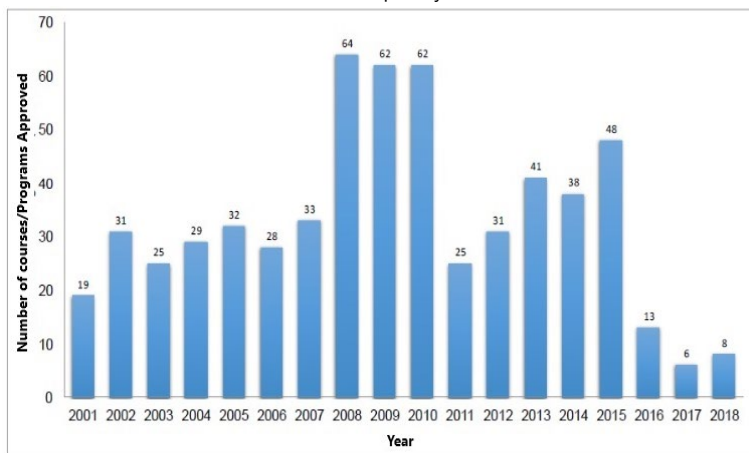
Interdisciplinarity in the health field represents a crucial paradigm for driving significant advancements in our ever-evolving society. In an increasingly complex, multicausal, and interconnected world, the challenges faced in the health sector are multifactorial and require integrated approaches that transcend traditional disciplinary boundaries. The convergence of various fields—such as medicine, information technology, speech therapy, physiotherapy, psychology, health management, medical physics, administration, chemistry, pharmacy, engineering, nutrition, and biology—enriches our understanding of health contexts and enables more effective and comprehensive solutions to complex problems. This holistic approach fosters a deep, qualified, and global understanding of specific issues.

Furthermore, the integration of diverse knowledge areas allows for the development of innovative technological solutions, including advanced devices, health information systems, and big data analysis methods for clinical and epidemiological research. Interdisciplinary collaboration can enhance our understanding of the challenges facing health systems, providing valuable insights to improve resource management, elevate service quality, and promote equity in access to healthcare.

The promotion of interdisciplinarity has been a priority for CAPES, recognizing its vital role in advancing research and academic training in Brazil. The goal is to foster collaboration across various fields of knowledge, encouraging the integration of diverse methodologies and approaches. Through interdisciplinary programs and initiatives, CAPES aims to enhance the academy's capacity to address contemporary challenges, stimulating the development of professionals with transversal skills and promoting innovative research that transcends traditional disciplinary boundaries (CAPES, 2019).

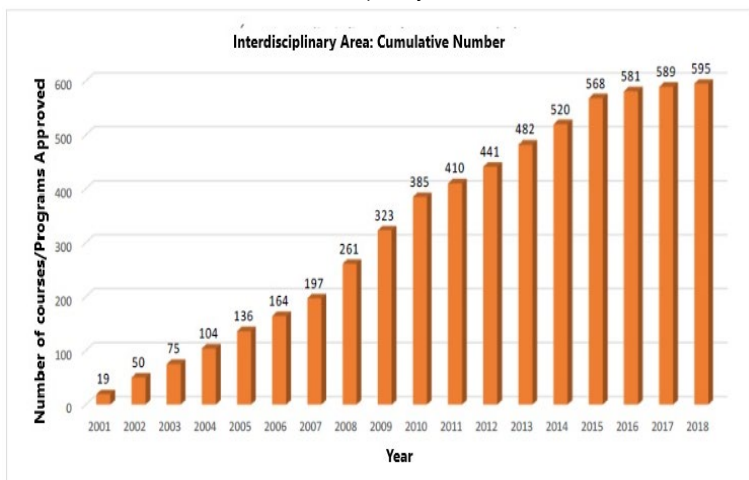
The approval of new graduate courses in the interdisciplinary area peaked between 2008 and 2010, while the most recent years recorded by CAPES (2016 to 2018) show significantly lower growth, as illustrated in Figures 1 and 2.

Figure 1. Evolution of the annual number of new Programs approved by CAPES in the Interdisciplinary Area.



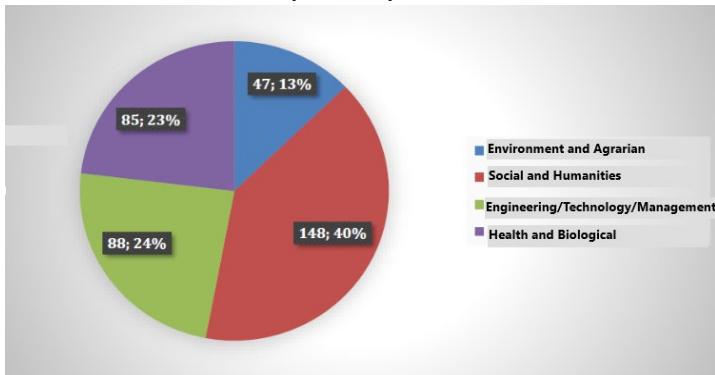
Source: CAPES, 2019.

Figure 2. Cumulative number of new Programs approved by CAPES in the Interdisciplinary Area.



Source: CAPES, 2019.

Figure 3. Distribution of Graduate programs in the Interdisciplinary Area recommended by CAPES, by Thematic Chamber.

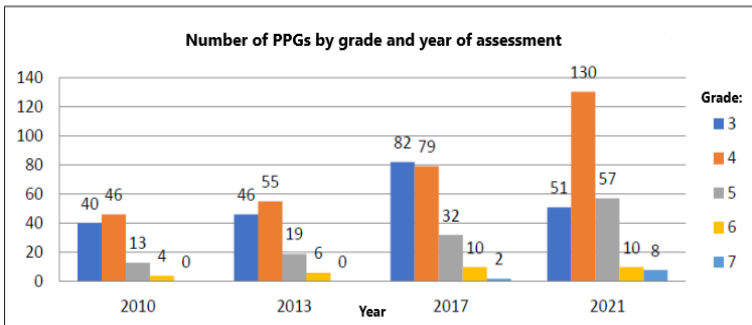


Source: CAPES, 2024

The Interdisciplinary Area has programs in all Brazilian states (Figure 5), distributed in its four Thematic Chambers (Figure 3). In all, there are 379 programs, 276 of which are academics (73%) and 103 professionals (27%) (CAPES, 2024).

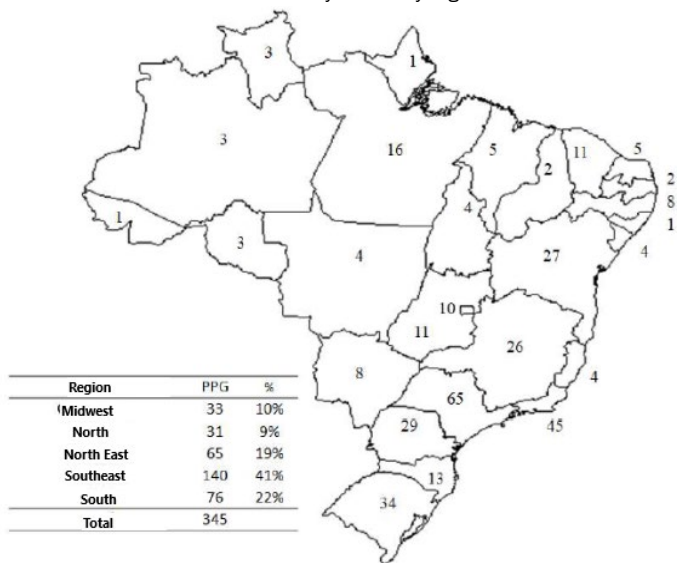
The programs in the interdisciplinary area show a trend of improvement in quality, as can be observed in an increase in the programs with all the best (Grades 4, 5 and 6), as can be seen in figure 4, which presents the evolution of the Academic Graduate Programs – 2010 to 2021 (CAPES, 2024).

Figure 4. Evolution of Academic Graduate Programs – 2010 to 2021.



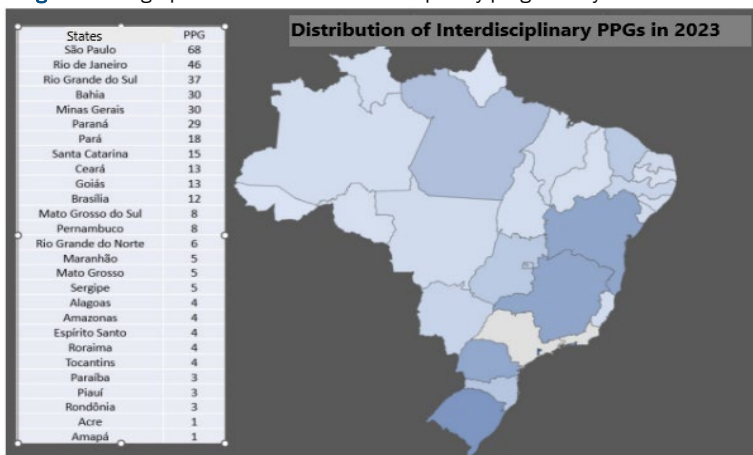
Source: CAPES, 2024.

Figure 5. Distribution of Graduate Programs in the Interdisciplinary Area recommended by CAPES by region.



Source: CAPES, 2024.

Figure 6. Geographic distribution of interdisciplinary programs by Brazilian state.



Source: CAPES, 2024.

20.3 Legacy of a Pioneering Interdisciplinary Graduate Program: PPGTIGSaúde

Between 2014 and 2015, the undergraduate courses in Biomedical Informatics and Health Management were launched at UFCSPA. In response to the needs and demands expressed by students in these and related fields, as well as by professionals in the market, a multidisciplinary group of faculty members began working to create a new graduate program (UFCSPA, 2024).

Research groups focused on "Intelligent Information Technologies" and "Health Management" at UFCSPA contributed to the development of this program proposal. These groups include faculty who are part of the core team of permanent professors and collaborators in the PPGTIGSaúde. The faculty's involvement in these research groups is evidenced by their intellectual output, including the publication of scientific articles, joint supervision of theses, and presentations at national and international scientific events. These collaborative activities enhance both academic and professional training, fostering the production of new knowledge in the program's area.

The PPGTIGSaúde at UFCSPA is part of chamber IV - Health and Biological in the interdisciplinary area and encompasses two areas of concentration: Intelligent Information Technologies and Health Management. The Intelligent Information Technologies area focuses on exploring the application of various information technologies in health, emphasizing the study, development, and application of Information Technology, Artificial Intelligence, Computational Intelligence, and Modeling and Simulation as tools for analysis and decision support in health contexts. Conversely, the Health Management area investigates techniques, methods, and standards related to health management, aiming to align technological use with the actual needs of managers while addressing strategic, tactical, and operational considerations to map processes and understand their complexities (UFCSPA, 2024).

The integration of these two areas will facilitate interdisciplinary teaching and promote advancements in health practices. The interplay between these fields is designed to foster a productive environment for collaborative and interdisciplinary research. The profile of the graduate student in the Graduate Program in Information Technologies and Health Management will be that of a qualified professional with a robust academic foundation, capable of acting critically, reflectively, and responsibly as a

multiplier in the field. These graduates will engage professionals, users, and the community, demonstrating competencies that include: Intervening in health practice situations by implementing transformative management and technological actions; addressing complex problems that require interdisciplinary knowledge in areas such as Computer Modeling and Simulation, Intelligent Systems, and Information and Knowledge Management; continuously monitoring and evaluating professional performance, promoting transformation through effective practices linked to the use of Information Technology and Health Management(UFCSPA, 2024).

Through these concentrations, PPGTIGSaúde aims to provide theoretical, conceptual, and methodological support to students, enhancing their capabilities with a more critical, reflective, creative, and innovative approach to research problems. This foundation will guide the preparation of Academic Master's dissertations that focus on scientific methods and critical analysis of results.

20.4 Challenges and Opportunities

Collaboration between different disciplines allows for a broader and deeper understanding of the social, environmental and economic determinants of health, contributing to the formulation of more effective and sustainable public policies, aligned with the Sustainable Development Goals, through the renewal and expanding of commitments to global sustainability, for the period 2015-2030 (ROME, 2019).

Figure 7. Sustainable Development Goals.

SUSTAINABLE DEVELOPMENT GOALS



Source: IPEA, 2018.

The goals can be described as follows:

- 01 - No Poverty: End poverty in all its forms everywhere;
- 02 - Zero Hunger and Sustainable Agriculture: End hunger, achieve food security and improved nutrition, and promote sustainable agriculture;
- 03 - Good Health and Well-being: Ensure healthy lives and promote well-being for all at all ages;
- 04 - Quality Education: Ensure inclusive, equitable and quality education and promote lifelong learning opportunities for all;
- 05 - Gender Equality: Achieve gender equality and empower all women and girls;
- 06 - Clean Water and Sanitation: Ensure availability and sustainable management of water and sanitation for all;
- 07 - Affordable and Clean Energy: Ensure access to affordable, reliable, sustainable and renewable energy for all;
- 08 - Decent Work and Economic Growth: Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all;
- 09 - Industry, Innovation and Infrastructure: Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation;

- 10 - Reduced Inequalities: Reduce inequalities within and between countries;
- 11 - Sustainable Cities and Communities: Make cities and human settlements inclusive, safe, resilient and sustainable;
- 12 - Responsible Consumption and Production: Ensure sustainable consumption and production patterns;
- 13 - Climate Action: Take urgent action to combat climate change and its impacts;
- 14 - Life Below Water: Conserve and sustainably use the oceans, seas and marine resources for sustainable development;
- 15 - Life on Land: Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, halt and reverse land degradation and halt biodiversity loss;
- 16 - Peace, justice and strong institutions: promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels;
- 17 - Partnerships for the Goals: strengthen the means of implementation and revitalize the global partnership for sustainable development.

These goals ultimately encourage researchers to frame their work within one or more of these objectives and to foster the training of future researchers with the knowledge and skills necessary to align their projects with these global efforts.

In this context there are a number of challenges, and at the same time, significant opportunities that allow scientific advances and professional qualification. Among the challenges are the effective integration of knowledge and methodologies of different disciplines and professionals, which mostly had a fragmented and contentist higher education with a priority emphasis on their formation in a unidirectional way. In addition, the diversity of perspectives and approaches of students and professors may require additional effort in building a collaborative environment and overcoming communication barriers.

Resource availability and financing can also be a challenge, especially for interdisciplinary programs that require advanced technological infrastructure and qualified multidisciplinary teamsteam. However, these challenges are accompanied by unique opportunities for innovation and

impact, which enable members of these programs to participate in a wide range of development edicts.

Consolidate research applied within the scope of PPGTIGSaúde: Contribute with the most diverse products of dissertations; Stimulate and develop the researcher's spirit in applied investigations; Promote scientific production through products arising from the production of master's students; Develop innovative training proposals that encompass the knowledge necessary for the development of skills and competencies within the scope of information technologies and health management.

The problems experienced in the daily life of societies reveal the opportunities and challenges needed to solve complex and urgent issues. In this regard, the importance of interdisciplinarity and working together brings the need for all to be aligned and work cooperatively.

For example, the recent catastrophe experienced in Brazil, specifically in Rio Grande do Sul, highlighted the urgent need for collaborative, solidarity, and resolution approaches. The flood required immediate medical attention and coordinated efforts on public health, logistics, environmental science, and social services to effectively manage. This disaster has demonstrated how interconnected knowledge of various disciplines is crucial to the comprehensive response and recovery of disasters. Effective management of such a complex situation involved not only the treatment of physical injury, but also addressing mental health concerns, ensuring infrastructure safety and sustainability, and future resilience planning. By integrating ideas and knowledge from different areas, it is possible to develop robust and adaptive strategies that can mitigate the impact of such disasters, make immediate decisions during different needs, and improve preparation for future events.

In this context, the use of Artificial Intelligence (AI) becomes particularly important. AI can improve predictive analysis, allowing early warning systems and more accurate prediction of natural disasters. During a crisis, AI-powered tools can facilitate the allocation of efficient resources, optimize emergency response efforts, victims' location, and animal care assistance, build support networks and reliable information, and support socket process decisions, providing real-time data analysis. After a disaster, AI can help assess damage, coordinate recovery operations, and even support mental health through intelligent virtual assistants. Incorporation of AI into interdisciplinary approaches not only increases the ability to respond to immediate needs but also contributes to the construction of more

resilient systems capable of supporting future challenges. This emphasizes AI's potential to transform interdisciplinary efforts, transforming challenges into opportunities for innovation, learning, and the advancement of social welfare.

20.5 Conclusion

The interdisciplinary area established by CAPES in the late 1990s has seen significant growth in both quantity and quality concerning postgraduate programs in Brazil. According to the Report from the Mid-Term Seminar of the 2021-2024 Quadrennium for the Interdisciplinary Area, the pandemic presented challenges to the full resumption of graduate activities, primarily due to physical and mental health issues reported by several program coordinators. These substantial transformations cannot be overlooked, and universities must undertake reform efforts in the short term to support the population affected by this period.

Research conducted by graduate programs indicates a decline in both student admissions and retention, as well as a decrease in publications by students and faculty, attributed to various multifactorial issues (CAPES, 2024).

Ultimately, the interdisciplinary area must analyze the challenges faced both in Brazil and globally. Collaborating with graduate program coordinators, it is essential to develop new solutions to ensure the advancement of this important and strategic area of knowledge in Brazil.

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Recommended Readings

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