DM

MERAKI - Virtual Reality System for application in Pediatric Oncology

MASTER DISSERTATION

Ana Filipa Rodrigues Gomes
MASTER IN INTERACTIVE MEDIA DESIGN

UNIVERSIDADE da MADEIRA
A Nossa Universidade
www.uma.pt

junho | 2021

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Master's Degree in Design and Media Interactive

Supervisor: Sergi Bermúdez i Badia
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Funchal, Junho 2021

Acknowledgments

First and foremost I would like to give my sincerest thanks to my advisor, Professor Sergi, for believing that I would be up to the task. Mainly for encouraging me throughout this long process and always having a positive word. I am very grateful for the opportunity I had to learn so much in the countless times we gather and for always being available to answer any questions and find solutions. Also, I would like to thank you for including me in the NeuroRehab Lab group, giving me the opportunity to learn from so many people who work there. Each meeting was a learning experience. None of this would be possible without your availability, understanding and humorous words of encouragement. I am very grateful for all the time you spent throughout this process.

To Professor Marlene for always being available to help.

To my mother who believes in me more than I do, who encourages me to always look for more and better and who, for me, is an inspiration and an example to follow daily. There are no words to describe how grateful I am to you for everything.

To Patrícia and Carlos who, in addition to everything they have already done for me, are the coolest bosses ever for streamlining every time I needed to leave work because of this project. Thank you for your patience and constant support. To my nephews for their honest critics and for encouraging me to do more and better. To my baby brother, Nuno, for the times he heard my complaints and doubts and advised me. To my Dad, and all my family members that somehow help me during this process.

To Antónia, thank you for everything. To Jordão, for his knowledge and for helping me with goals that seemed impossible to achieve. To Laura and João, for the team spirit and companionship over these two, sometimes difficult, years. I Couldn't have asked for better classmates than both of you.

Last but not least, to César, who lived my daily joys and frustrations and who always had a friendly hug for me. For always making me look for the silver lining, for believing in me every day and for never letting me give up. Thank you very much for your patience and tolerance. I am very grateful to have you in my life.

To all children around the world who have to face a cancer diagnosis.

Resumo

O cancro pediátrico continua a ser a maior causa de morte nas crianças em Portugal. Por ano registam-se cerca de 400 novos casos. Os tipos de cancro mais comuns são Leucemia e Linfoma de Hodgkin. A média de idades com mais casos é entre os 10 e 12 anos. O período de tratamento pode variar entre meses a anos, consoante o caso. A quimioterapia é um dos tratamentos mais utilizados para tratar estes dois tipos de cancro. A duração e o número de sessões é ajustada consoante a gravidade da doença e pode durar entre 10 minutos a várias horas por sessão. Uma das queixas mais frequentes das crianças é a fatiga e a duração dos tratamentos.
As atividades mais frequentes durante este período de tratamento incluem brinquedos, jogos de consola e televisão. Contudo, a criança não consegue abstrair-se do ambiente hospitalar e está alerta para todos os sinais sonoros e visuais que ocorrem à sua volta.

Nesta dissertação, proponho a criação de um jogo em realidade virtual como método de distração da dor. A utilização de um “head-mounted display” sem fios permite que a criança passe a estar num ambiente virtual distinto do ambiente do tratamento, que tenha liberdade de movimentos e uma vez que o aparelho inclui colunas de som embutidas permite, também, a abstração dos sons característicos do ambiente hospitalar. Este estudo tem como objetivo a criaçãp de um ambiente em realidade virtual, pensado para utilização em Occulus Go, recorrendo a uma experiência com a duração mínima de 20 minutos onde, para progredir no jogo, é necessário completar tarefas,

Palavras-chave: Realidade virtual, Tratamento de cancro pediátrico, Distração da dor.

Abstract

Pediatric cancer remains the leading cause of death in children in Portugal. There are about 400 new cases per year. The most common types of cancer are Leukemia and Hodgkin's Lymphoma. The average age among most cases is between 10-12 years. The treatment period can vary from months to years, depending on the case. Chemotherapy is one of the most used treatments to treat these two types of cancer. The duration and number of sessions are adjusted depending on the disease's severity and can last from 10 minutes to several hours per session. One of the most frequent complaints of children is fatigue and the duration of treatments.
The most frequent activities during this treatment period include toys, console games, and television. However, the child cannot abstract himself from the hospital environment and is alert to all the audible and visual signals.

In this thesis, I propose creating a virtual reality game as a method of pain distraction. A wireless head-mounted display that allows the child to be in a virtual environment distinct from the treatment environment, with freedom of movement. Since the device includes built-in speakers, it also enables the abstraction of the hospital environment's sounds. This study aims the creation of a virtual reality system, using unity 3d, designed for Occulus Go. Resorting to an experience lasting at least 20 minutes where along the way it is necessary to fulfill tasks to progress

Keywords: Virtual reality, Pediatric cancer treatment, Pain distraction.

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Acronyms

VR - Virtual Reality
HMD - Head Mounted Display

1. Motivation

In this chapter, I will start with the motivation for using virtual reality in pediatric cancer treatments. I will also describe the main goals of this study.

In Portugal, it is estimated that 400 new cancer cases appear each year, which is the leading cause of death in children. This problem affects not only the child but all family members, who are too devastated after receiving such a diagnosis.

In our society, games play an essential role in children's daily lives, so it seems very natural to use them as serious games for pain distraction[1], relaxation, and reducing patient's anxiety[2]. Over the years, with the rapid growth of technology, there was also some interest in introducing them in the context of hospital treatment[3], namely in the relief of pain[4] of people injured with severe burns[5], in the minimization of anxiety before a medical procedure, and a search for the relaxation of adults undergoing treatments for different types of cancer. Even though there is access to new technology, the studies published still use large equipment, with wires and at prices not so accessible, which makes access to these proposals difficult.

Considering that few studies have been conducted on using virtual reality as an ICT approach for children undergoing cancer treatment, it is an area that should be further investigated. This study intends to be a step in that direction. This thesis aims to show what was done as adjunctive therapy to chemotherapy treatment to understand each strategy's advantages and disadvantages.

1.1. Research Questions and Methodology

This study aims to assess if virtual reality with the use of on the market equipment, can be useful as a pain distractor. For this, it would be necessary to create a game that was visually appealing, where the child felt motivated to play and was challenging enough to distract from the hospital environment.

RQ1: Is there potential in using Virtual Reality as a distractor of pain?

RQ2: Can Virtual reality be more effective, if it is specially designed for pediatric oncology treatments?

RQ3: What characteristics should this system have to be effective?

RQ4: For the development of an application, what elements should be implemented to address this issue?

1.2. Contribution

This study's primary goal was to create a more economical and accessible solution using virtual reality as a pain distraction for children undergoing oncological treatments [6]. This serious game was designed for pediatric oncology patients to be used in any hospital or clinic.

This tool was created from scratch using Unity 3D software and Oculus Go. To guarantee the feasibility of this study, it was necessary to cover the following issues:

- The game had to be used on Oculus Go;
- It must fulfill the requirements of an immersive game;
- Tasks must be designed for the target audience;
- Must have as little equipment as possible and should be wireless.

With this work and through the literature review carried out, it was found that there is a gap in the use of virtual reality in pediatric oncology to minimize pain through distraction, which can be explored.

1.3. Document Structuring

This document is divided into four chapters and as follows: Chapter 1, Motivation, research questions and contributions of this thesis; Chapter 2, State of the art, Prevalence of pediatric cancer in the world, Europe and in Portugal, its symptoms, diagnosis, and treatments; Chapter 3, System development with software implementation, proposal, hardware setup, and final proposal; Chapter 4, Conclusion with a discussion of final results and future work.

2. State of the art

Introduction

This chapter is dedicated to all the work that has been done so far in the area of virtual reality as a tool for distracting pain[7] . To obtain the most recent data possible, the research was done, looking for articles less than ten years old that were listed on Google Scholar and PubMed. The following keywords were used: pain distraction, cancer treatments, virtual reality, virtual reality as medical treatment, virtual reality for pediatric cancer treatments.

2.1. Prevalence of pediatric cancer in the world, Europe and Portugal

The fast pace of the population's growth and aging show cancer's prominence as a leading cause of death worldwide.

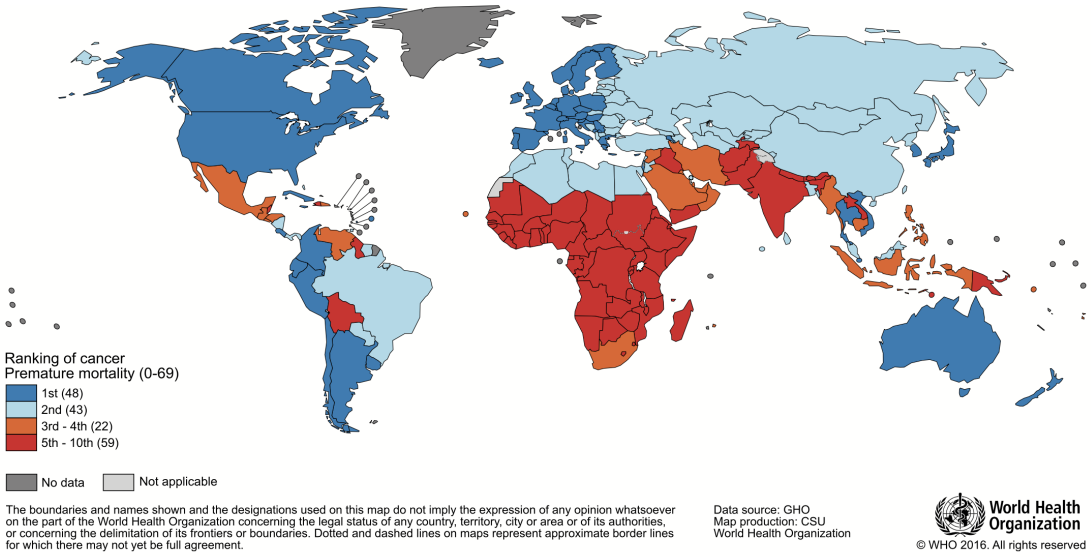


Figure 1 - Global Map with National Ranking of cancer as a cause of death at ages below 70 years in 2015. Source: World Health Organization[8]

Bray et al. estimated that in 2018 there would be 18.1 million new cases and 9.6 million cancer deaths worldwide [9]. Europe will account for 23.4% of the cancer cases and 20.3% of the deaths.

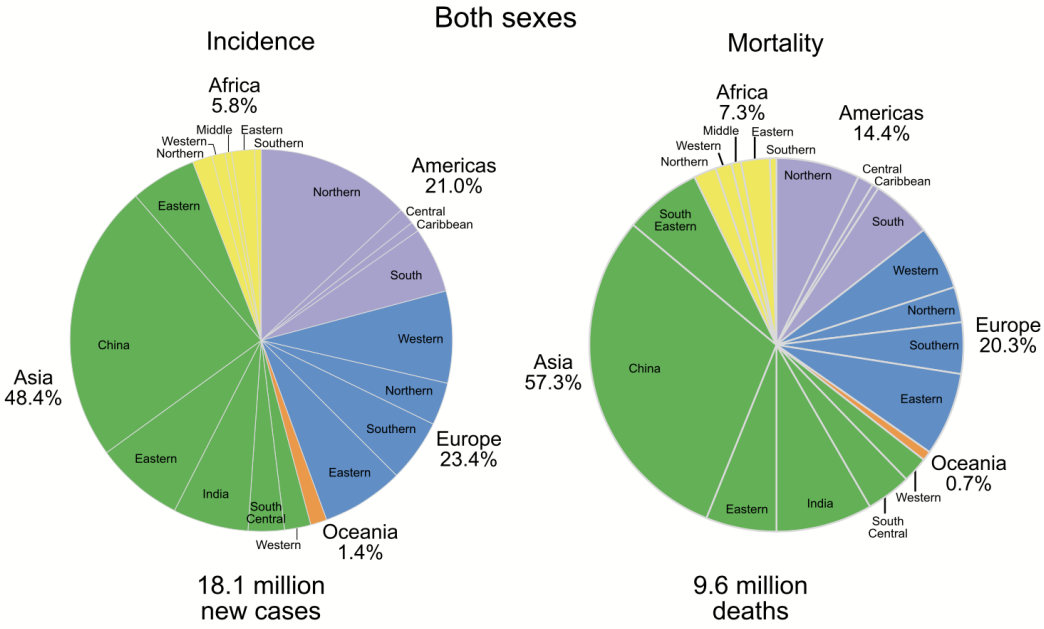


Figure 2 - Pie Charts represent the distribution of cases and deaths by World Area in 2918 for Both sexes. Source: GLOBOCAN, 2018 [1].

A broad important cause of morbidity and mortality is cancer, predicting that 1 in 8 men and 1 in 10 women will, in a lifetime, develop the disease[10]. The different types of cancer emerge according to the regions' specificities and are related to social, economic, and lifestyle changes.

More recent studies reveal that one-third to two-fifths of new cancer cases could be prevented if exposure to risky lifestyles and environments already known as such are eliminated or minimized[2].

With this information, I was guided by European data that included Portugal, from 2010.

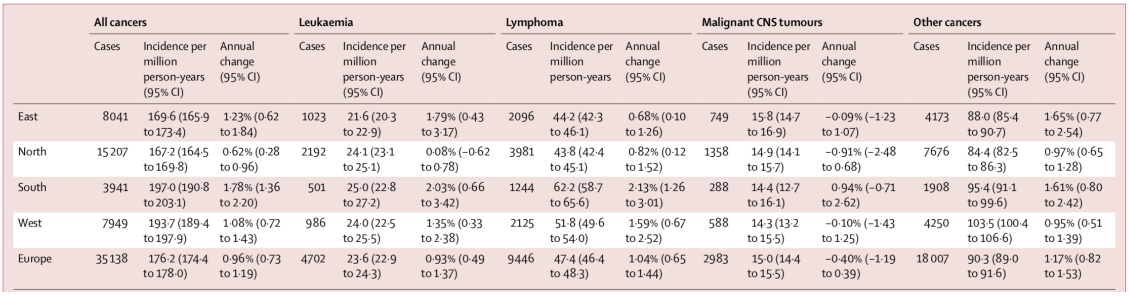
	All cancers			Leukaemia			Lymphoma			Malignant CNS tumours			Other cancers		
	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)
South	14 450	149·9 (147·4 to 152·3)	0·40% (0·07 to 0·72)	4472	47·3 (45·9 to 48·7)	0·68% (0·17 to 1·18)	2137	20·4 (19·5 to 21·2)	0·29% (−0·54 to 1·11)	2317	23·9 (22·9 to 24·8)	−0·44% (−1·24 to 0·37)	5524	58·3 (56·8 to 59·9)	0·57% (0·06 to 1·08)

Figure 3 – Number of new cases, world age-standardized incidence per million person-years, and average annual percentage change by diagnostic category in children aged 0-14 years, by European region, 1991-2010. Source: GLOBOCAN, 2018

In South Europe, the number of new cases, within the age range of 0 to 14 years and between the years 1991-2010, was 14,450 cancers in general. There were 4472 cases of Leukaemia, 2137 of Lymphoma, 2317 of Malignant CNS tumors and 5524 cases of other cancers.

We can then say that the most common types of cancer in children between 0 and 14 years, within the years of 1991 and 2010 were:

- Malignant CNS tumors;
- Leukaemia;
- Lymphoma.



	All cancers			Leukaemia			Lymphoma			Malignant CNS tumours			Other cancers		
	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)	Cases	Incidence per million person-years (95% CI)	Annual change (95% CI)
East	8041	169·6 (165·9 to 173·4)	1·23% (0·62 to 1·84)	1023	21·6 (20·3 to 22·9)	1·79% (0·43 to 3·17)	2096	44·2 (42·3 to 46·1)	0·68% (0·10 to 1·26)	749	15·8 (14·7 to 16·9)	−0·09% (−1·23 to 1·07)	4173	88·0 (85·4 to 90·7)	1·65% (0·77 to 2·54)
North	15207	167·2 (164·5 to 169·8)	0·62% (0·28 to 0·96)	2192	24·1 (23·1 to 25·1)	0·08% (−0·62 to 0·78)	3981	43·8 (42·4 to 45·1)	0·82% (0·12 to 1·52)	1358	14·9 (14·1 to 15·7)	−0·91% (−2·48 to 0·68)	7676	84·4 (82·5 to 86·3)	0·97% (0·65 to 1·28)
South	3941	197·0 (190·8 to 203·1)	1·78% (1·36 to 2·20)	501	25·0 (22·8 to 27·2)	2·03% (0·66 to 3·42)	1244	62·2 (58·7 to 65·6)	2·13% (1·26 to 3·01)	288	14·4 (12·7 to 16·1)	0·94% (−0·71 to 2·62)	1908	95·4 (91·1 to 99·6)	1·61% (0·80 to 2·42)
West	7949	193·7 (189·4 to 197·9)	1·08% (0·72 to 1·43)	986	24·0 (22·5 to 25·5)	1·35% (0·33 to 2·38)	2125	51·8 (49·6 to 54·0)	1·59% (0·67 to 2·52)	588	14·3 (13·2 to 15·5)	−0·10% (−1·43 to 1·25)	4250	103·5 (100·4 to 106·6)	0·95% (0·51 to 1·39)
Europe	35138	176·2 (174·4 to 178·0)	0·96% (0·73 to 1·19)	4702	23·6 (22·9 to 24·3)	0·93% (0·49 to 1·37)	9446	47·4 (46·4 to 48·3)	1·04% (0·65 to 1·44)	2983	15·0 (14·4 to 15·5)	−0·40% (−1·19 to 0·39)	18007	90·3 (89·0 to 91·6)	1·17% (0·82 to 1·53)

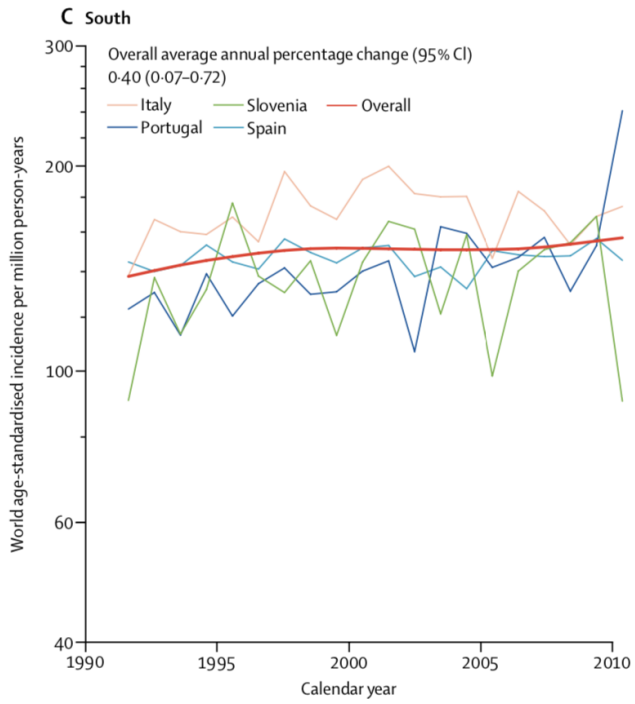
Figure 4 – Number of new cases, age-specific incidence per million person-years, and average annual percentage change by diagnostic category in adolescents aged 15-19 years, by European region, 1991-2010. Source: GLOBOCAN, 2018

In South Europe the number of new cases, within the age range of 15 to 19 years and between the years 1991-2010, was 3941 cancers in general. There were 501 cases of Leukaemia, 1244 of Lymphoma, 288 of Malignant CNS tumors and 1908 cases of other cancers.

We can then say that the most common types of cancer in children between 15 and 19 years, within the years of 1991 and 2010 were:

- Lymphoma,
- Leukaemia;
- Malignant CNS tumors;

After analyzing these graphics, we can say that in South Europe between the years 1991 and 2010, there was a higher incidence of cancers in the ages between **0 and 14 years**.



Number of new cases, world age-standardized incidence per million person-years, and average annual percentage change by diagnostic category in children aged 0-14 years, by European region, 1991-2010

Figure 5 – Incidence trends of cancer in children aged 0-14 years in Europe, 1991-2010. Source: GLOBOCAN, 2018

According to this figure that shows the incidence trends of cancer in Europe between 1991 and 2010, in children within an age range of 0 to 14 years, Portugal has not fled the average.

In Portugal, there is no database with information on the number of existing cases. The Rui Osório de Castro Foundation, however, says that there are about 400 new cases of pediatric cancer in Portugal, per year. It also tells us that the registration of new cases is being implemented and that in the future there will be a database.

2.2. Symptoms, diagnosis

According to the Portuguese Leukemia Association (PLA), Hodgkin's Lymphoma is the most common type of lymphoma and comprises four subtypes with different histologies.

Hodgkin Lymphoma

Hodgkin Lymphoma is a malignant tumor of the lymphatic system that occurs when there is a malignant transformation of lymphocytes. Of these four, two stand out, most predominantly in a young population:
*"Sclero-nodular - **About 60-70% of cases** occur particularly in **younger people** and are slightly more frequent in females; has a better prognosis with a high chance of cure. The ganglion has a thickened capsule and a nodule-like interior. Fibrous nodules may persist after treatment. Usually, the disease is limited.*

*Mixed cellularity - **About 25% of cases** often occur in **children** and the elderly. In the ganglion are several different cells and many Reed-Sternberg cells. In this type of LH, the disease is usually widespread, with general symptoms and immunity compromised. The possibility of cure is high."* [10]

This type of malignant disease arises due to alterations of some genes that have under their control the development of cells.
In some lymphomas, there may be an association with some infections, prolonged contact with toxic substances, or situations of immunosuppression such as in transplant or HIV patients, but in most cases it is not known what causes these changes. We can state that this is not an inherited or contagious disease. PLA estimates that in Portugal there will be 300 new cases per year with higher frequency in men between 16 and 25 years old.

The appearance of enlarged - mostly painless lymph nodes - in the neck region, armpits and less often in the groin, is the most common symptomatology of this lymphoma. Size increase of the ganglia in the mediastinum, an area between the lungs, is also frequent. There may be abdominal discomfort or pain caused by enlarged liver and spleen. In this lymphoma, involvement of other organs is less frequent compared to non-Hodgkin's lymphoma. People with this lymphoma may develop other symptoms such as fever changes that oscillate without the use of medication, night sweats, fatigue, weight loss, body itching, skin changes. A hematologist will make a correct diagnosis through a ganglion biopsy, blood tests, radiographs, computed tomography (CT), positron emission tomography (PET), electrocardiogram (ECG) and bone marrow evaluation by myelogram and bone biopsy.

Through the Ann Arbor Staging, it is possible to assess the extent of the disease before treatment. For an assessment of the disease stage, this system is based on the area in which it is located, the number of affected regions, and the absence of systemic symptoms (fevers, weight loss, absence of symptoms. The stages range from I to IV and are described as follows:

Stage I
Lymphoma is located in only one lymphatic region.

Stage II
Lymphoma is located in 2 or more lymph node groups on the same side of the diaphragm.

Stage III
Lymphoma is located in the areas of lymph nodes above and below the diaphragm and may include the spleen.

Stage IV
Lymphoma has spread widely in at least one organ outside the lymphatic system, such as bone marrow, liver, or lung.

Treatment of Hodgkin lymphomas may include chemotherapy and radiotherapy. The clinical condition and type of diagnosis, along with the doctor's opinion and the patient's will, will dictate the most appropriate treatment type.

Side effects can be controlled and, in most cases, are reversible. There are more frequent symptoms that result from these types of treatments. Patients in treatment usually experience **fatigue and lack of appetite.** Some patients undergoing chemotherapy need to receive blood transfusions due to the worsening of anemia caused by this type of treatment. It is also very common for the patient to feel **nauseous and vomit**, but the use of proper medicines can alleviate these symptoms.
There is a greater risk of infections, as this treatment causes a decrease in white blood cells. Even for this disease, one of the most frequent causes of death is pneumonia. The patient may feel **pain or a burning sensation on the skin** due to an infection (*Herpes zoster virus*) commonly called ‘Zone’. As a result of this treatment, the patient's **skin becomes very sensitive**.

Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is a malignant disease of the blood that occurs due to the excessive production of lymphoblasts, which do not reach mature cells. The rapid multiplication of these cells causes the bone marrow to become full, preventing the production of other normal cells. As there is a decrease in white blood cells and platelets, anemia arises.

This disease is more common in children, and 60% of cases occur before age 20. About 107 new cases appear each year in Portugal.

Some symptoms appear quickly, such as anemia, infections, and rapid bleeding, but only with a complete blood count is it possible to make a correct diagnosis. Yet, a bone marrow biopsy may even be necessary.

Acute leukemia has several subtypes that will be determined by different gene changes. The specific type of disease will condition response to treatment. However, the most commonly used treatment that should be started as soon as the disease is diagnosed is chemotherapy associated with cortisone. Chemotherapy cycles include various medications and are given in-hospital (internment). For the body to recover, this treatment is done in several cycles, every few weeks. Chemotherapy is administered through a central catheter placed in a larger caliber vein, such as the subclavian vein, which is below the clavicle.

Factors such as age, ALL subtype, and cytogenetic changes, i.e., “risk group” assessment, will define the type of chemotherapy. However, the treatment consists of several phases and has a total duration between 2-3 years:

- In the first phase, the objective is to induce remission, which consists of eliminating leukemia cells and average marrow recovery.
- Second phase: Consolidation - After remission is achieved, further chemotherapy cycles are required to prevent relapse.
- There may be a phase between the 2nd and 3rd that is called intensification and will only be used for some more aggressive types of ALL, where more intensive chemotherapy will be given.
- After consolidation, chemotherapy treatment is administered orally and by some periodic intravenous administrations of certain cytostatic; this is called the Maintenance phase - Third phase.

In the early stages of treatment, hospitalization is required until the spinal cord recovers from chemotherapy’s effects; the 3rd phase - maintenance, is done on an outpatient basis.

Side effects are very similar to Hodgkin's lymphomas, can be partly prevented and controlled by medication, and are mostly reversible as well. It should only be mentioned that there is a greater risk of bleeding due to decreased platelets, and therefore it is advisable to avoid possible injuries and falls.

2.3. Primary treatments

Primary therapy is the one accepted as the best treatment, when used by itself. For cancer patients, a standard set of treatments, is usually surgery followed by chemotherapy and radiation. The type of treatment varies depending on the type of cancer and how advanced it is[11] . The child's age and other existing health conditions are also factors that influence the procedure.

Chemotherapy

This treatment stops or slows the growth of cancer cells, using medications. Most cancer cells divide rapidly, and as chemotherapy destroys cells that are in the process of dividing there is a greater chance of successfully eliminating them with this treatment.

The disadvantage is that, as most drugs go through the bloodstream, it ends up destroying some types of healthy cells throughout the body.

Chemotherapy is done in cycles formed by a treatment cycle and a rest cycle and can be administered in four possible ways: through an intravenous; oral route; as an injection or as topical chemotherapy. In general, common side effects of chemotherapy may include mouth sores, fatigue, nausea, diarrhea, hair loss, anemia, and increased risk of infection.

Radiation

This treatment uses high-energy radiation to reduce tumors by destroying cancer cells. The most common type of radiation therapy used to treat cancer in children is external beam radiation. Other types include internal radiation therapy and systemic radiation therapy.

As with previous treatment, radiation therapy also affects healthy cells. However, side effects vary depending on the area where radiotherapy is being performed and can occur as skin irritation and fatigue.

2.4. Adjunctive therapies

In a search for the patient's well-being and the reduction of stress and anxiety levels, alternative therapies have been found that can be combined with the primary treatment. The analysis of these adjunctive therapies[12] allowed us to understand what is being done in the treatment centers and what types of interactions have the most positive results.

2.4.1. Non-ICT driven approaches

Guided imagery

In 2005, Roffe collected and analyzed data of guided imagery as an adjuvant cancer therapy [13] and concluded that the patient's comfort can be better, however, there is not enough data to show positive effects on the physical symptoms resulting from this type of treatment.

Traditional Chinese Medicine

Liao[14], in 2017, due to the fact that traditional Chinese medicine is considered one of the most popular alternatives to cancer treatment, evaluated in a study with about 23,803 cases, whether combining this therapy with conventional cancer treatment could improve the survival rate of lung cancer patients.

This study demonstrated that traditional Chinese medicine can be an adjunctive therapy, not only for lung cancer, but for other types of cancer.

2.4.2. ICT driven approaches

In 2005, Wolitzky et al. l. work described that several studies have proven that distraction can be highly effective when used as a successful intervention for children undergoing invasive medical procedures[15] . The main advantage of using a VR system as a distraction technique over watching tv, or playing traditional games has to do with the head-mounted display being able to reduce the awareness of other people and the hospital surrounding. The HMD creates a more immersive[16] and interactive setting for the patient[17]. However, more research is needed on its effects, especially in pediatric populations, due to the minimal sample size interventions. Wolitzky intervention consisted of a VR system that allowed children to visit the gorilla habitat at zoo Atlanta, in which the patient was able to explore the environment.

To better understand the result of the intervention, the following tools were used: - How-I-Feel questionnaire (Spielberger, Edwards, Montouri & Lushane, 1970[18]) to measure the anxiety levels; Pulse-oxygen monitor (BCI International, Waukesha, WI); Visual Analogue Scale for pain and anxiety (VAS, Varni, Walco & Katz, 1989) and The children’s hospital of eastern Ontario pain scale (CHEOPS, McGrath, et al., 1985). It concluded that VR was effective in decreasing distress and pain behavior during the procedure.

Susan M. Schneider, in 2011, concluded that VR could make chemotherapy treatments more tolerable with the advantage of being a noninvasive intervention[19] . Also mentioned that anxiety and negative expectations are related to worse treatment-related adverse effects that

can trigger negative impacts on chemotherapy administration, such as anticipatory nausea. Chemotherapy can trigger unpleasant emotions like fear, anxiety, and sadness when the patients observe their own treatment or that of others. Interventions such as humor, music, and movies have been used as a pain distractor for patients receiving chemotherapy. Also, relaxation and imagery can give patients some control over the experience. The downside of these techniques is that they are only effectively deployed if the patients can learn and practice them before the first session, and there will be a need to master the techniques. VR can help reduce acute pain, anxiety, distress[20] and can be a promising intervention since it prevents external stimuli, taking them away from the hospital environment[21]. Using VR as a distraction allowed healthy children and adults to tolerate experimentally generated ischemic pain for more extended periods[22]. Being fatigue, one of the most frequently reported side effects of chemotherapy, its impact; also, previous studies showed that using VR during these treatments makes them more enjoyable and well received by patients. Patients considering the time elapsed shorter than the actual time are more likely to be pleased with this treatment.

In 2019, Eijlers et al. collected and analyzed several studies on “Virtual Reality in Pediatrics: Effects on Pain and Anxiety” Stated that having a feeling of presence in the virtual environment can create full immersion [23], and more immersion is related to pain reduction since there is less attention available for pain perception. Results showed that VR interventions for pain reduction were more efficacious for younger children. In this meta-analysis it was demonstrated, by 14 studies for pain and 7 for anxiety, that VR is a useful tool to lower patient-reported pain and anxiety during a range of medical procedures. The effect of VR on pediatric pain was also significant when observed by caregivers and professionals [24].

The vast majority of studies using virtual reality focus on pain reduction for patients who have suffered severe burns[25]; there is no significant sample of studies with virtual reality designed for pediatric oncology patients.

2.5. Summary

It is possible to conclude that younger children tend to have higher levels of anxiety[26] before medical procedures[27]. Due to magical thinking and imaginative play, VR is especially engaging for younger children[28] when used as an intervention for pain reduction. Diverting the attention away from noxious stimulus and focusing on more pleasant stimuli results in a reduction of the perception and experience of pain. The use of an HMD, in a study, can bring a sense of presence by having the environment changing in real-time, along with the user’s

moves. Given that visual perception has an impact on brain mechanisms and influences motor function and pain sensation the decision to resort to virtual reality as a pain distractor for patients undergoing chemotherapy treatment, seems very appropriate and becomes a main advantage, as the objective will be, for a few minutes, to lead the imagination of these children from the hospital environment and being able to get them to abstract themselves for moments of the treatment they are doing.

VR does not require practice prior to use in the clinical setting; therefore, it is possible to have interventions with more successful results.

3. Iterative Design Process

This chapter describes the creation and implementation of the game in virtual reality to be used in Oculus Go. This section is a detailed description of the initial sketches development to the final result with all the implementation choices taken. The conceptualization of the game is also described at the end of this chapter.

3.1. Proposal

For the development of this game, I looked for elements for creating outdoor environments with nature, with the main purpose of contrasting with the hospital environment and taking players to a different reality from the one they are experiencing.

Influenced by the Minecraft[29] trend, I knew I wanted a game in which objects would also look "blocky" and that allow the player a free exploration of the game, without the need to meet strictly defined times or objectives. I also knew that I wanted the game to be played from a first person perspective.

Figure 6 - Minecraft in action, images from the Official website.

In order to define the scenarios, it wascreated a moodboard with images taken from google that demonstrated what was intended for this project. There was a search for elements of nature such as trees, flowers, rivers, etc. in order to later be able to create a scenario with a magical forest, where surprise elements could be inserted such as: the need to create a bridge to be able to cross to the other side of the river.

Figure 7 - Moodboard for the scenarios, images from google

After gathering some images, there was some creation of prototypes of scenarios, which were evaluated by the supervisors, changed according to the feedback, and to what was intended for the final result. It was a cyclical process until we found the desired result considering the time frame available to create and present the proposal.

3.1.1. Aesthetics

Low Poly seeks to highlight the idea that a composition of shapes can represent the world; this style of game aesthetics can be found in popular games of the moment. Polygons can, in theory, have any number of sides but are commonly broken down into triangles for display. Objects that are low poly often appear blocky and straightforward while still maintaining the basic shape of what they are meant to represent. In the game industry, this style is also popular

since it serves the dual purpose of reducing development time and giving the game a unique aesthetic technique.

After some research and the idea of contrasting the closed environment where children do their treatments. I came to the conclusion that I wanted outdoor environments with nature as the central theme. Some sketches were made with samples of the scenario to be replicated.

3.1.2. Game mechanics

This is a simple game, from a first-person perspective, designed for the player to interact with and can be broken down into two game mechanics:

- Puzzle solving, to progress in the game, the player must place the colored cubes on the corresponding color platform.
- Mobility, while moving through the game, the player encounters several cubes.

3.2. Setup

To use this game, the player will need Oculus Go and some free space around, so that the player can move freely, since he will be using a head mounted display and will see an environment completely different from the one he is physically in.

3.2.1. Hardware

In many of the studies carried out previously, it was found that the chosen equipment was not practical to transport, required a desk computer, it was necessary to have wires to make the connection between the virtual reality equipment and the computer. Chemotherapy treatment itself already requires the presence of cables and tubes, so the idea would also be to minimize the visual aspect concerning this issue.
The equipment used for this project is Oculus Go. It is a standalone VR that, due to the fabrics and mold injected foam, becomes light and comfortable since the straps that hold the glasses are adjustable.
The sound provides an involvement with the player because it has built-in spatial audio controllers into the straps providing immersive sounds. Oculus Go also has a motion controller that can be used to interact with apps and games.

Figure 8 - Oculus Go

3.2.2. Software

Content creation for Oculus Go will be done through Unity. It is a very useful software that enables us to build for several platforms like PC, console, web, VR, and AR. Unity asset store provides 3d models, animations, audio, and shaders. This tool is one of the leading extensive platforms for developing games, with vast popularity in the game world's development industry and is completely free.

A significant advantage of Unity is that it allows the use of PlayMaker, since this feature allows to create games without having to code. Hutong Games developed it, and it uses finite-state machines (FSM) to easily add physics, animation, interactive objects, and scene changes. The FSM can change from one state to another in response to some inputs. An FSM is defined by a list of its states and the inputs that trigger each transition.

I had already used Visual Studio, which is a source code editor developed by Microsoft for Windows, Linux and macOS, in previous small projects, and since I don't have a lot of experience with this type of software, I chose to continue with this one.

To create content for Oculus GO, it was necessary to use Android Studio and after installation, configure XR Settings to 'Virtual Reality Supported'. There was also a need to install Android Debug Bridge (ADB) and the drivers for the Oculus Go, which is a versatile command line tool that allows communication with a device.

3.2.3. Assets

Unity has an Asset Store that makes available a library of assets. An asset can be an audio file, an image, or a 3D model created outside of Unity. These assets are created by Unity

Technologies and community members who create and publish them in the store. It is possible to find various types of assets, from textures, animations and models. It is possible to buy assets, but some of them are free, both can be downloaded directly from the Unity Project.

For this project I used assets with low poly elements, which were related to the theme that was intended.

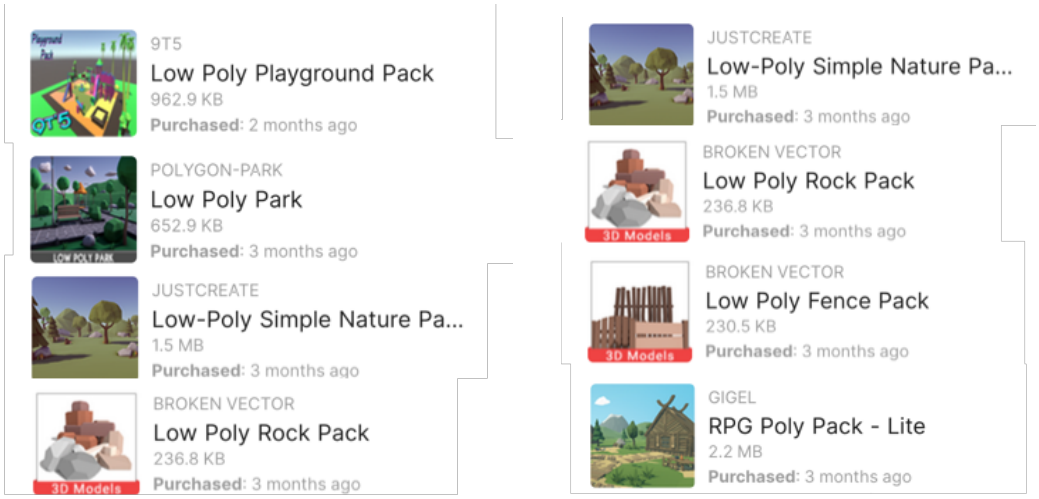


Figure 9 - Assets used on the project

3.3. Implementation

For the implementation of this game, it was first necessary to understand what types of cancer affect children in Portugal the most, what are the treatments, what side effects they bring and what adjunctive therapies exist.

Secondly, it was necessary to review the work that used virtual reality as a pain distractor and understand if the participants reported nausea or other discomfort when using this type of technology.
After gathering data, it was necessary to think about what this game consisted of, what would be the visual approach, what mechanics would be used, duration and gameplay. Then, in a cycle of trial and error, the game was being adjusted and rethought as difficulties arose.

3.4. Requirements

After visiting the pediatric ward of Hospital São João with the co-supervisor of this project, where we had the opportunity to speak with the ward head-doctor and head-nurse, and along

with some data collected, it was concluded that in order to guarantee the feasibility of this study, it was necessary to cover the following issues:

- The game should work on Oculus Go – since it is a wireless equipment, commercially sold and therefore affordable.
- The game should be aimed at pediatric oncology patients between the ages of 8 to 10 years - since it is in this age spectrum that the largest number of cases occurs in Portugal.
- The content must be designed for virtual reality - because with this equipment, the player no longer sees the hospital context in which he finds himself and only sees the image that is in Occulus Go.
- The game must be possible to be played between 20 minutes to several hours - through research, it was realized that chemotherapy sessions can last from 20 minutes to several hours, so it would be important to create a virtual reality system that could be used by all patients, regardless of the duration of their session.
- The game should abstract the player from the hospital environment - One of the reasons for the increase in stress and anxiety in carrying out cancer treatments is the fact that the patient is surrounded by other patients who are going through the same process or worse;
- The game must not be complex. The game should not have negative emotional aspects. The game should not have a “game over” or loss of game lives - Going through the process of overcoming a cancer is difficult enough. The game created cannot increase frustration and anxiety in the player. The goal is to help.

3.5. Low fidelity prototype

In this first scenario, the intention was to create a warm and familiar environment in a garden with benches, a bandstand, trees, and flowers.

For this, I used existing assets in the Unity Asset Store, with elements in low poly that represented nature.

Figure 10 - First prototype of the first scenario

The second environment is a small village in the mountains it was created with some assets equal to the previous scenario and with some different ones, like the huts.

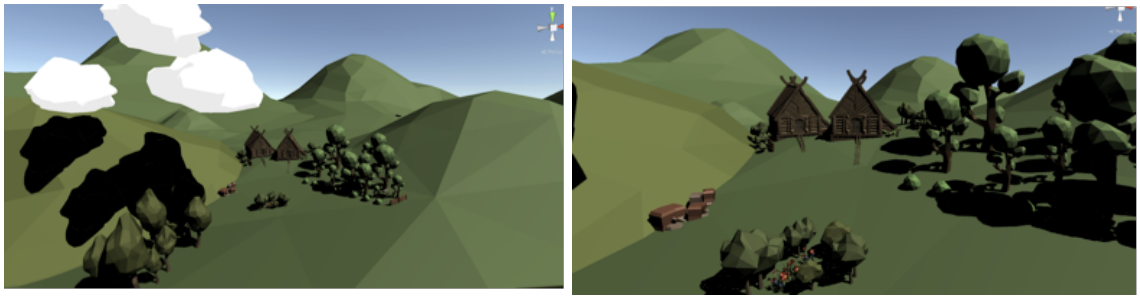


Figure 11 - First prototype of the second scenario

The third environment, a small village in the mountains, with picnic benches and a forest area.

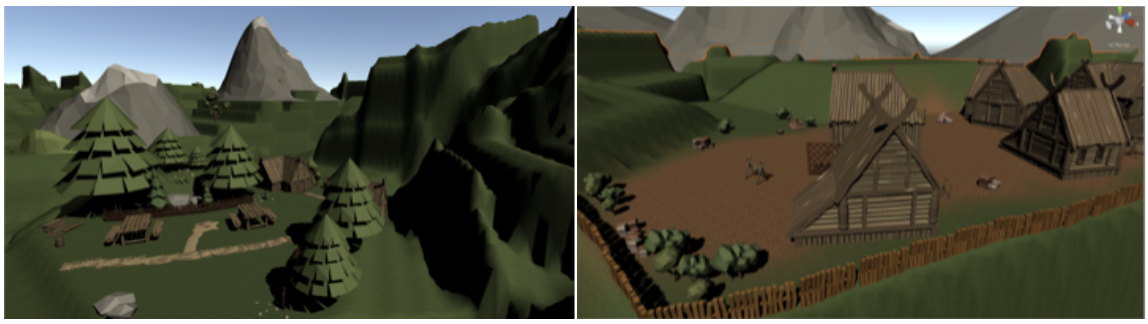


Figure 12 - Scenes from the Village scenario

After these first sketches, it was concluded that the scenario lacked color, were untidy, and the environment was dark.

Since the second and third scenarios had few different aspects from each other, it was decided that there should be only one scenario with the combination of these elements.

3.6. System development

There are, as we have seen in the state of the art, countless forms of entertainment for treatment processes, not only for cancer, but for diseases in general. What we found is that there is not much research regarding virtual reality and pediatric cancer treatment. The aim of this study is to bridge this existing gap and open the way to an area that deserves to be further explored. Virtual reality has helped in the abstraction of the patient while undergoing painful procedures[30] [31]. So, with this study, we will seek to combine virtual reality with the distraction of pediatric patients' pain through the development of a game with wireless, commercial and affordable equipment, making it possible to use it in different social contexts.

The first step was to find out which equipment is best for this purpose, since It should be wireless so as not to interfere with the existing wires during the treatment process, lightweight and comfortable because many of these patients already have very sensitive skin, easy to integrate and commercially available. For all these reasons, the chosen equipment was the Occulus Go. The integration of the virtual reality system with the equipment was made using Unity 3d software.

This Virtual Reality project is called Meraki. A Modern Greek word, derived from the Turkish “Merak” (Labor of love, to do something with pleasure), is applied to tasks, usually creative or artistic tasks. It means to do something with passion, with absolute devotion, with undivided attention.

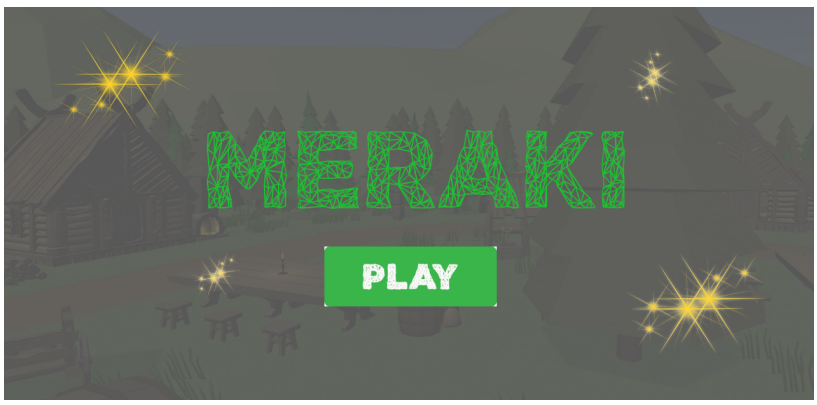


Figure 13 - Opening image of the game

This game was designed to be an immersive experience of discovering an outdoor setting, to act as a pain distractor for children undergoing chemotherapy treatments. Along the way, the player encounters interactions that allow progress in the game. Including these tasks, we direct the player's focus and give a simple goal: accomplish each of the interactions and discover the game.

Below is a simplified outline of the game.

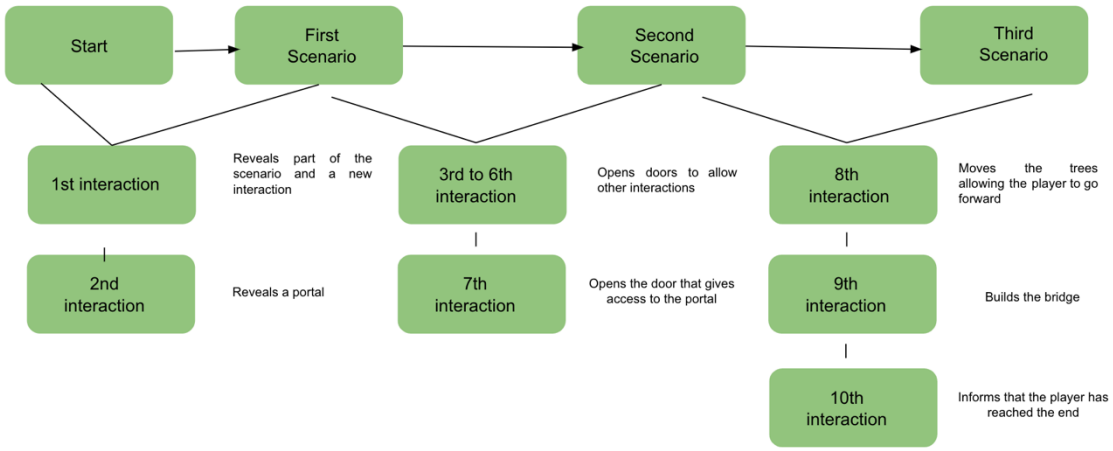


Figure 14 - Outline of the game

In the game there are some elements with different functions, which are explained below:

Start button - this button allows the player to start the game.

Cubes - In the first scenario, a cube and platform with a corresponding color appear. This cube is responsible for the interaction during the game, along the scenarios. When placing the cube on the right platform, it triggers the following actions:
- Appearance of hidden objects;
- Appearance of a portal that allows the transition to another scenario;
- Opening doors.

Platforms - The platform gives the player an indication that the cube must be dragged there. This component appears in all scenarios, and its function is the same in all of them.

Play again button - When the player reaches the end of the game, he has the possibility to return to the beginning and start the game.

Quit - When the player reaches the end of the game and does not want to continue playing, he can leave the game.

3.6.1. Iterations and changes

First iteration

Knowing in advance that the game would be based on an outdoor environment, the creation of a mountain scenery started, with elements of nature. This scenario had a raised floor, giving an idea of the existence of hills and valleys. Here, it was thought that the player would explore the environment freely.
It was concluded that the dimension of the scenario was extremely large, that the lack of interactions could turn the game into a boring experience because there was no objective for the game.

Second iteration

It was thought that the ideal would be to have several scenarios, or the creation of different environments within a single scenario, in order to make the experience more interesting, with the discovery of different elements.

After some attempts to make a scenario with different environments harmonious, several scenarios were created with different elements but always with the outdoor environments with elements of nature as a theme. These environments still did not have much diversity in terms of color and luminosity.

Third iteration

In order to make these scenarios more colorful, elements were introduced in the park, to make it a playground with a slide, swing and similar objects. The colors of the trees were also modified in order to make them distinct, and the light was worked to make the scenario brighter. Existing more than one scenario, it was necessary to understand the best way to make the player pass between them. Thus, portals were created, which the player found throughout the scene while walking to explore it

Fourth iteration

Once the scenarios were defined in terms of objects and color, it was thought that the creation of tasks would be essential to motivate the player and keep the focus on the game. For that purpose, colored cubes and platforms of the same color were placed so that the player had to place the cube on the corresponding color platform.
It was thought that this interaction with the cubes could have an effect, for this, the portal is hidden and only appears when the interaction is done correctly.

Fifth iteration

In order not to make this system repetitive, other action results were considered after the interaction.
Thus, throughout the scenario there are cubes that make objects appear in a descending or ascending way, others that are hidden and appear, there are new cubes appearing that allow the game to continue, trees that move away so that the player can continue and there is the cube that ends the game and allows the player to play again.

3.6.2. Final prototype

Having the need to add tasks to make this experience a game, and not just a video of nature elements, there was a need to remodel the scenarios to create more controlled environments.

This game developed is divided into different scenarios, namely: playground, village, and magic forest. The creation of these scenarios arises from the need to create a game that lasts at least 20 minutes so that patients with different treatment durations can experience it. Different scenarios will work as a surprise element, creating the expectation of what will come later. The main objective would be to introduce interactions throughout the scenario to keep the player engaged with the game, acting as a distractor for the small activities that the player would have to perform.

Interactions within the scenario have different results, which will be explained in more detail in the next lines. In the appendix there is the code that complements the images below.

In order to start the game, there is a menu, which displays the name of the game and contains a button to start the game.

Figure 15 - Start menu

This menu is created with an object called Canvas, which is used for images, buttons and texts. An image has been placed on this object and a button.

First scenario – Playground:

This scenario aims to take children to a reality that they already know but that they have not been able to visit since they are under treatment. It is a nature setting, with a playground with elements such as slide and swing.

After pressing the start button, the player encounters the first scenario, the player is placed inside a bandstand and can see some trees, a colored cube and a platform of the same color.

The goal is that the player's first instinct is to push the object to the base. The character applies force to the object, making it move. As soon as the object is on top of the platform, two animations will appear.
First, a colored area with a slide, and then a new object (cube) will appear on the stage. When the cube collides with the platform, the animations are activated.

The following images demonstrate the previous description.

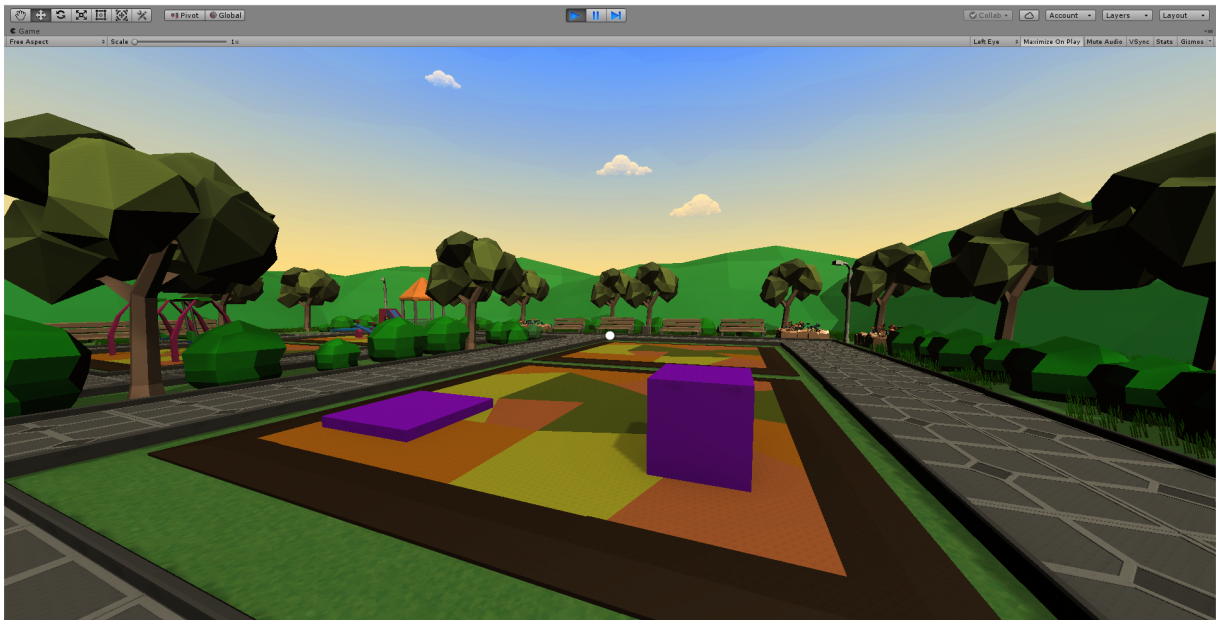


Figure 16 - First scenario with the cube and the platform

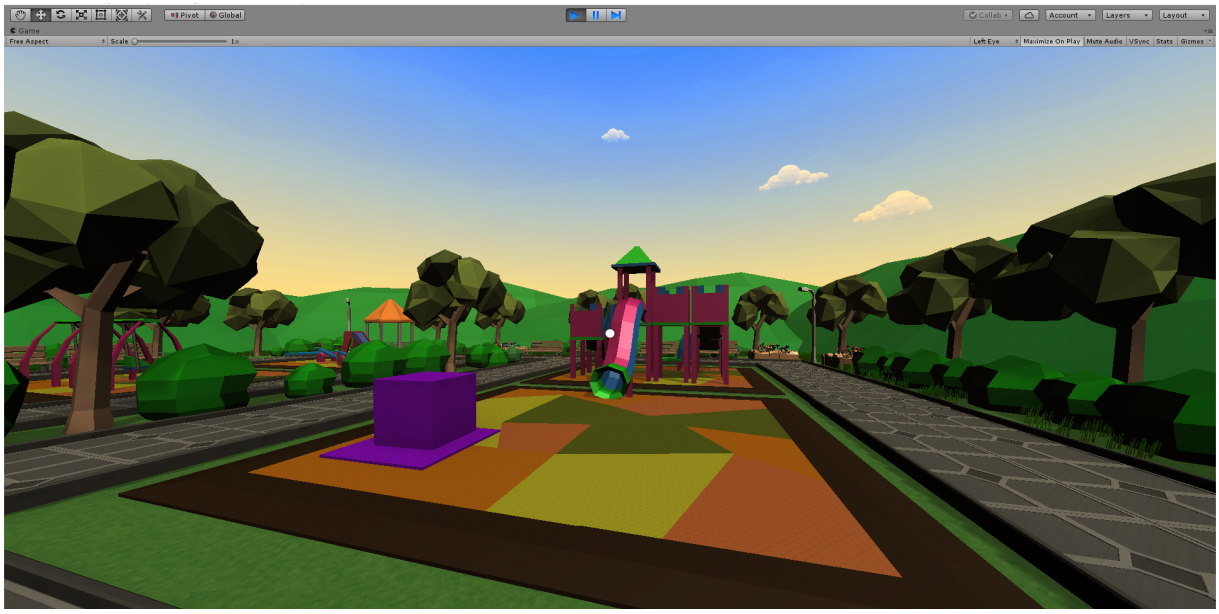


Figure 17- Scenario after the interaction

With the new cube that emerged after the first interaction, the player will have to position it on a new platform to open a portal for another scenario.

Figure 18 - Scenario previous the second interaction

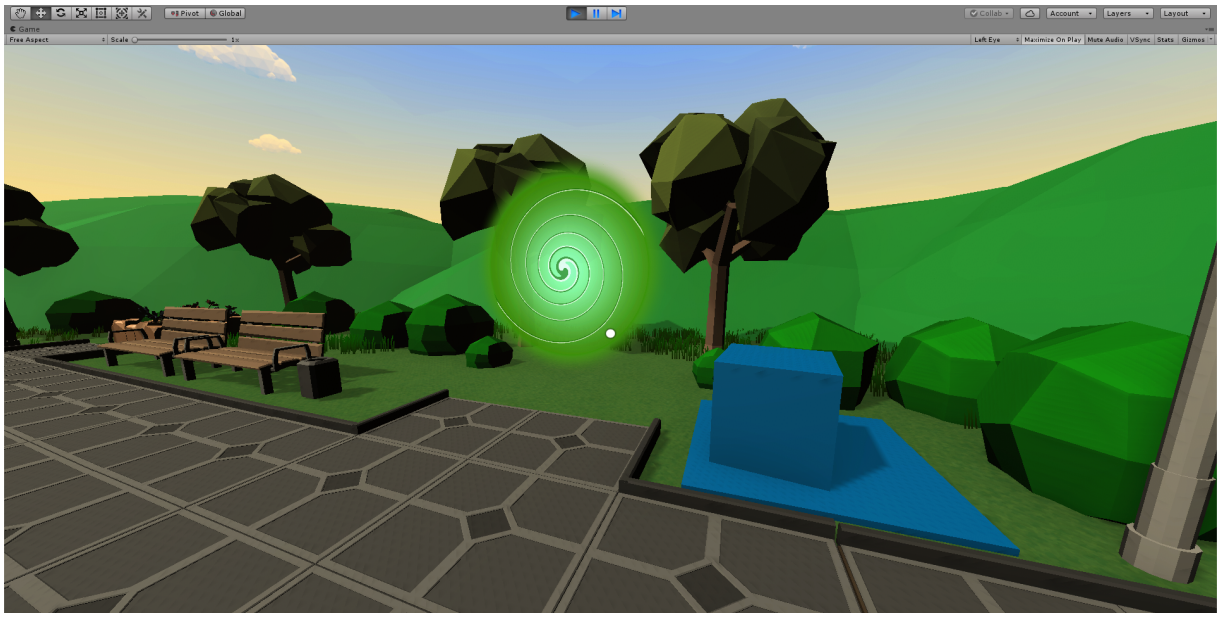


Figure 19 - Scenario after the second interaction

With the portal already active, the player will be able to pass through it. This way, the player will be "teleported" to another scenario.

Second Scenario - Village:

This scenario consists of several huts and is surrounded by trees. In the center there is a small lake. Once in the new scenario, the player will find several gates.

The player will have to place each cube on a platform with the corresponding color to open these gates.

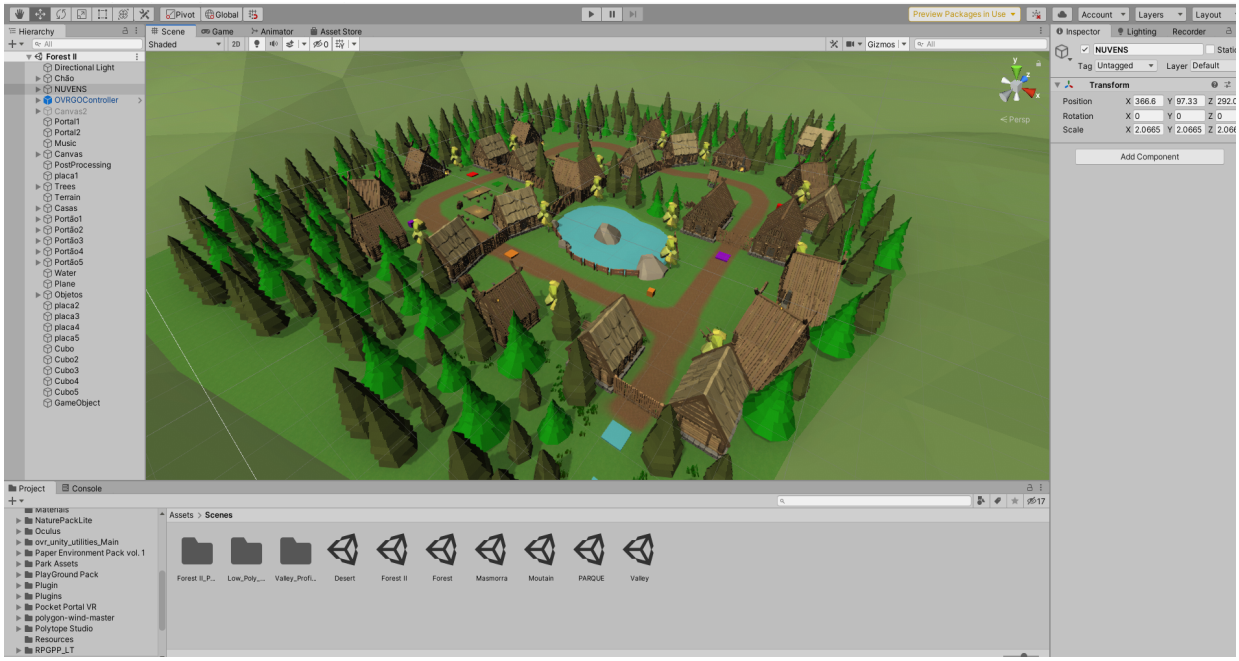


Figure 20 - Overview of the scenario

In the image above we can have a complete view of the second scenario.

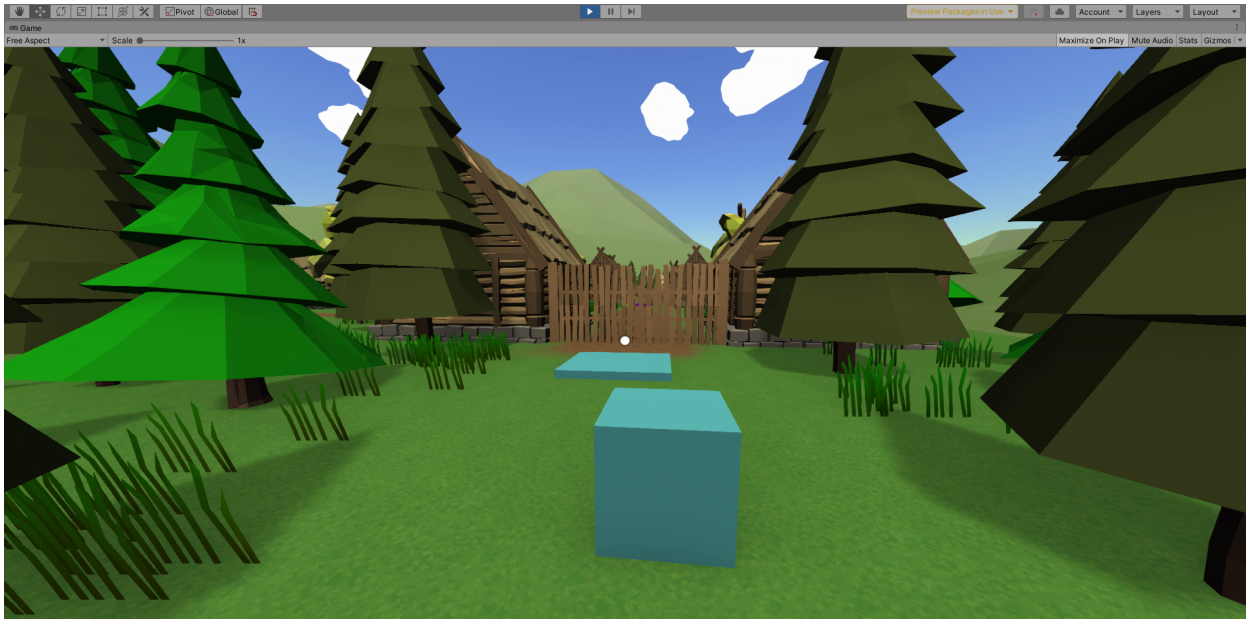


Figure 21 - First interaction in the second scenario

In the image we see above, there is the first interaction of the second scenario. The player must place the cube on the platform in order to open the door that allows him to continue playing.

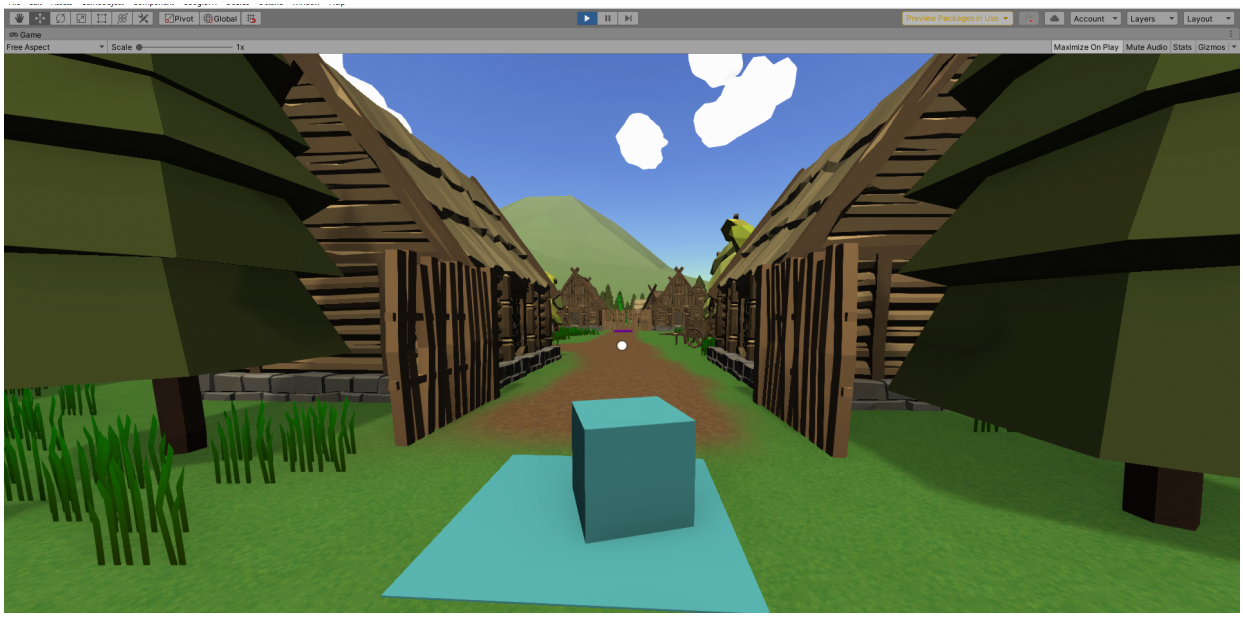


Figure 22 - The result of the interaction.

The image above shows the result of the player's interaction with the cube. The door opens and the player can continue his journey.

In order to transition to the third scenario, the player needs to interact with another cube and after opening the last gates, a new portal opens for another scenario.

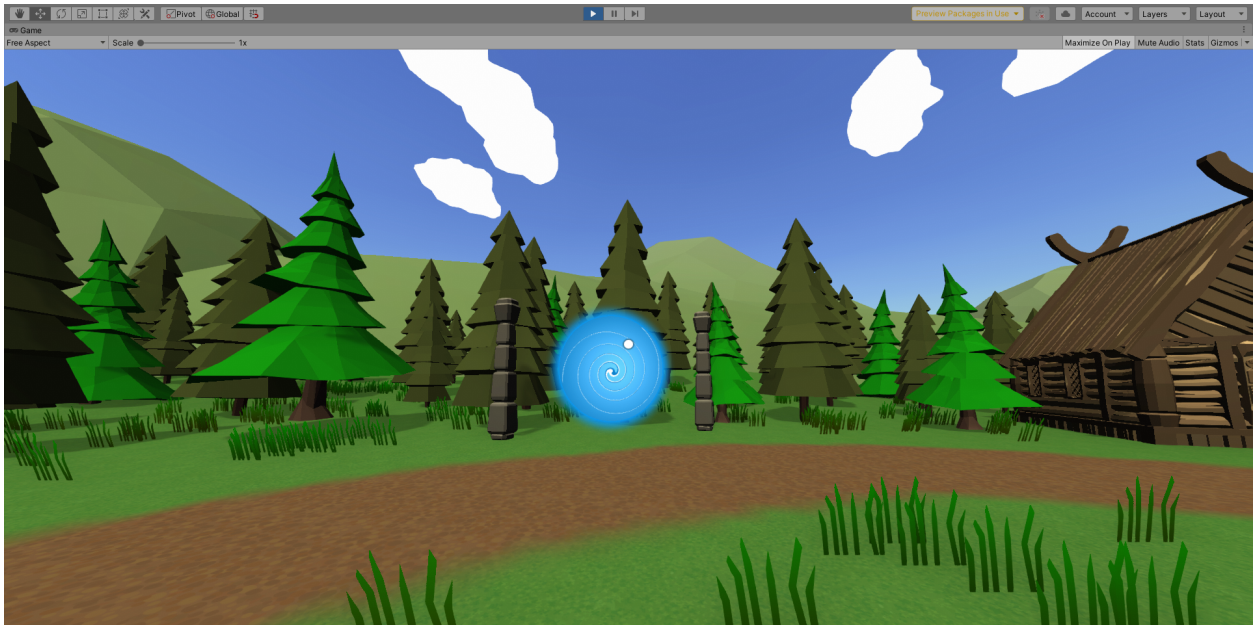


Figure 23 - The new portal.

Above, we can see the portal that appears with the last interaction in the second scenario and that allows the user to make the transition to the third scenario.

This forest, at first glance, is not so magical, as it has elements similar to the previous scenarios, but the first interaction will turn it into the magic forest.

Upon reaching the new scenario, the player will encounter several obstacles in a forest (incomplete bridges, trees). To pass the obstacles, the player will have to place the cubes on the platforms with the corresponding colors.

Figure 24 - Scenario with the obstacles.

The obstacles in the third scenario are found in the image above and below. In the image above, we see the passage covered by rocks and trees and below we see the unfinished bridge that does not allow the user to continue his journey.

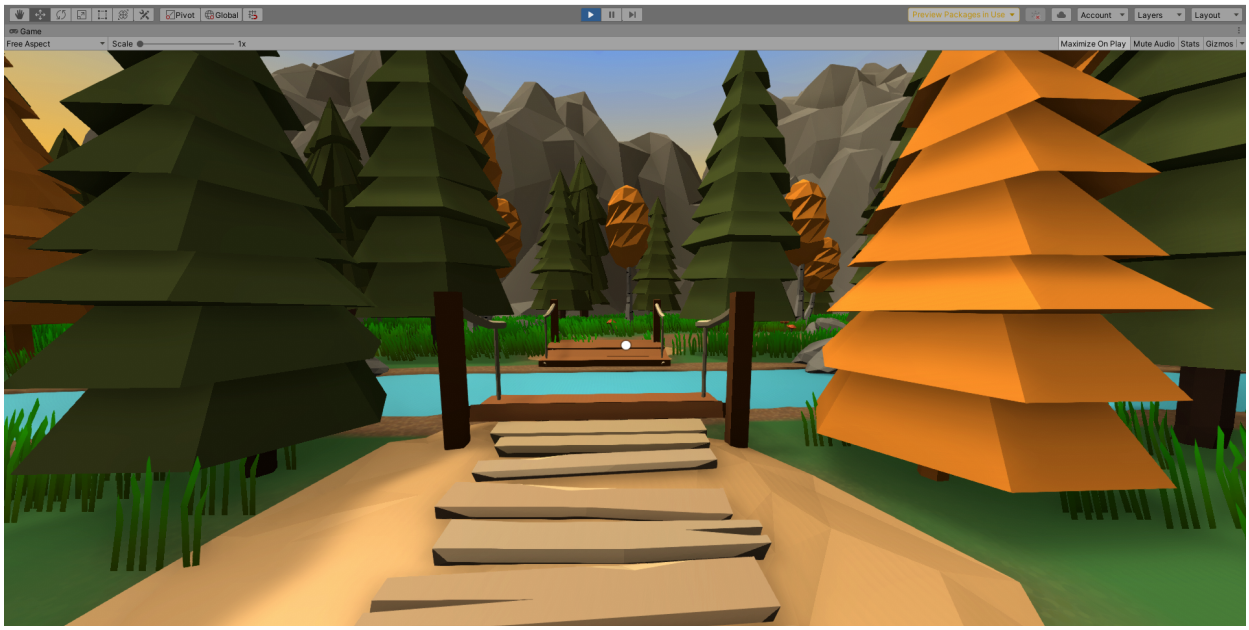


Figure 25 - Scenario

When the player interacts with the cubes, he manages to cross the Forest, as the trees and rocks move away and in the second interaction, the missing part of the bridge arises through the river and makes the bridge complete allowing the passage.

In the image below, we can see the result of the player's interaction with the red cube. Before there were trees and rocks preventing the passage, but with the interaction, there was a withdrawal from these elements allowing the player to continue.

Figure 26 - Scenario after the interaction

The image below shows the cube placed in the correct position and the result of this interaction. The bridge is now completed, and it is now possible for the player to continue playing.

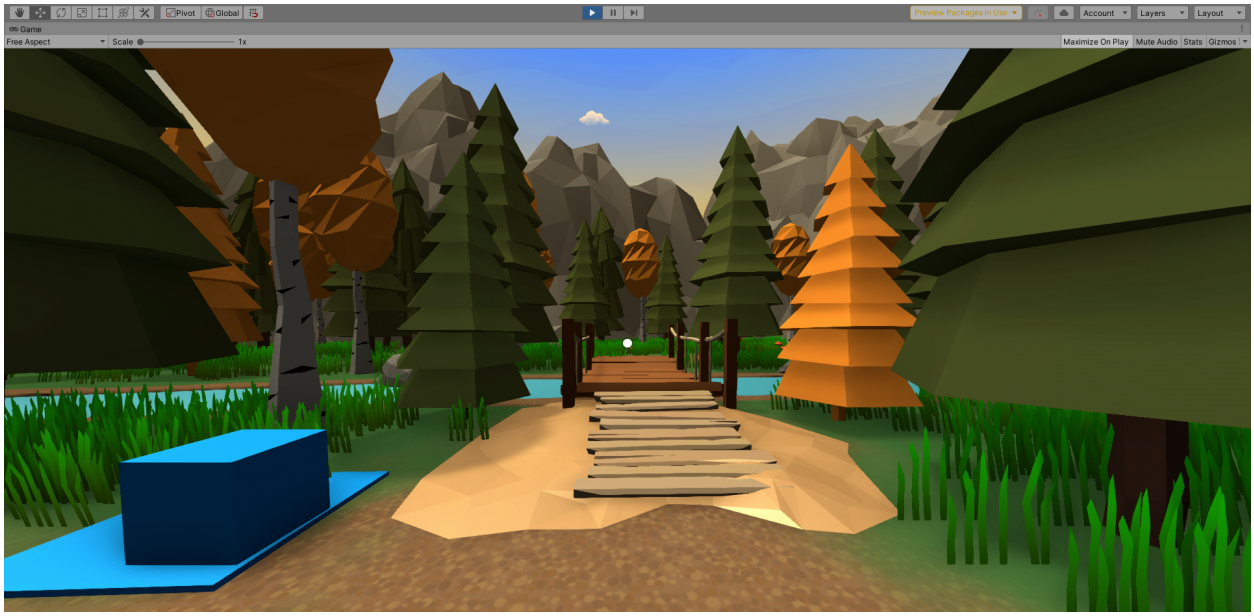


Figure 27 - Scenario with the interaction completed

Below we can see the last interaction with the cube.

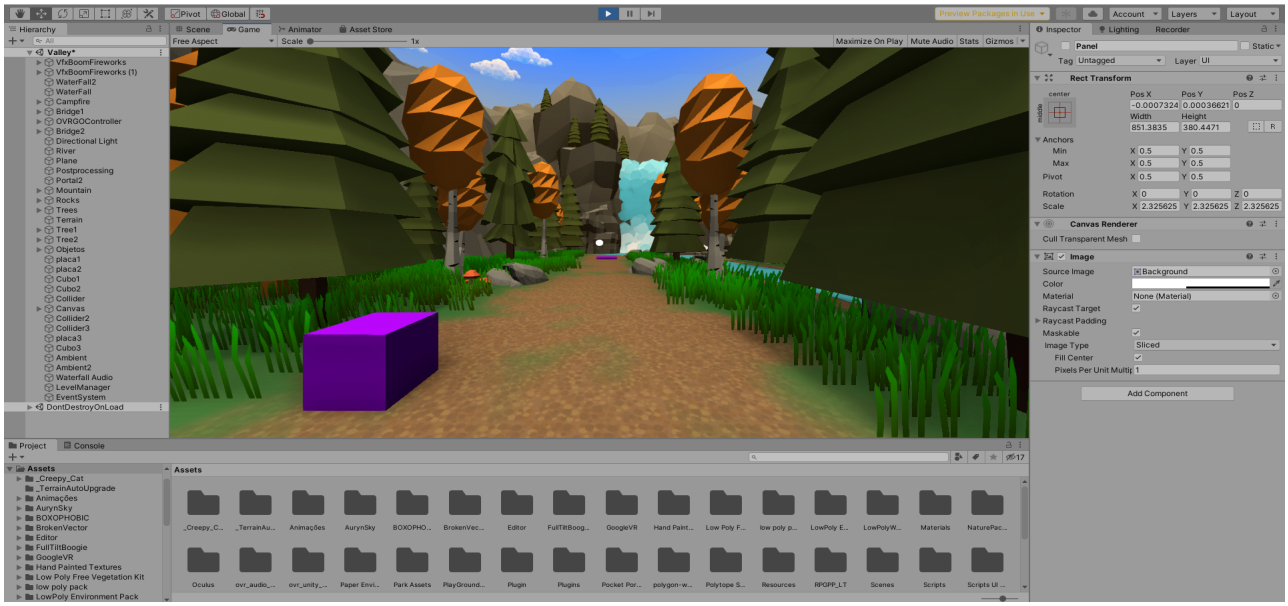


Figure 28 - Scenario with the last interaction

When placed on the corresponding platform, an animation with several fireworks starts and then a message of "Well Done" and two buttons (the canvas is used here again).

Figure 29 - The result of the last interaction

One of the buttons will restart and the other will exit the game.

Summary

This game consists of three scenarios: playground, village and magic forest.
In the first scenario, there are two interactions. The first, unveils part of the scenario and reveals a new interaction. The second reveals a portal that gives access to the second scenario.

In the second scenario, we find five interactions along the way, which allow us to open doors. The last interaction opens the door that gives access to the new portal.

Magical forest is the last scenario. Here we first find an interaction that allows trees and rocks to move so that the player can continue the course. Then, there is an interaction that allows to build the bridge so that is possible to cross to the other side of the river and find the last interaction that tells us that the game is over and asks us if we intend to play again or leave the game.

4. Conclusions

Cancer is the leading cause of death in Portuguese children. Virtual Reality can help reduce the anxiety and stress related to cancer treatments. This dissertation reviews the state of the art of ICT driven approaches, specifically the ones that use virtual reality for pain distraction and brings to evidence some opportunities that the virtual reality system created aims to fill. The intention is not to replace treatments but to make them more tolerable and less painful.

This work sought to understand the relevance that virtual reality can have as a pain distractor from pediatric oncology treatments, using a game created for Oculus Go - a wireless, light and easy to acquire technology - that takes the player to a different reality than the one he is experiencing, through a journey of outdoor environments full of nature.

The main reason for choosing outdoor environments was the contrast with the cold and serious environment in which children are carrying out their treatments. The intention was to be able to get players to abstract themselves from the hospital environment, making them complete tasks so that the focus is totally on the game.
From the first sketches to the final result, alterations occurred in order to complete the scenarios with green, colorful elements, inserted in a luminous environment with the feeling of being outdoors.
The head mounted display, becomes the great advantage of virtual reality, compared to other therapies designed for the same effect, since it allows the player to be completely immersed in the game.

- Research Questions & Answers

RQ1: Is there potential in using Virtual Reality as a distractor of pain?
Since one of the limitations of this work was related to the impossibility of performing user tests, only with future work we will be able to answer the question.
RQ2: Can Virtual reality be more effective, if it is specially designed for pediatric oncology treatments?
This question needs also need user tests in order to give a complete answer. However, it seems clear to me that when an experience or game is designed from scratch, taking into account the issues of a specific theme, the final result will be, certainly, better than a game or experience created for a general audience.
RQ3: What characteristics should this system have to be effective?

According to the literature, one of the ways to make this system effective would be to make it possible for the player to abstract himself from the hospital environment that surrounds him during treatment. The literature also demonstrates that the elements of nature have effects capable of reducing anxiety, making the treatment process less difficult for the patient.
Keeping the player focused on a task is also validated by the literature as a way to abstract the patient from the treatment process.

RQ4: For the development of an application, what elements should be implemented to address this issue?
The use of virtual reality would be a point in favor since after placing the equipment, it only allows the player to visualize what is presented by the glasses.
Elements of nature such as mountains, trees, waterfalls and flowers were inserted in this system, to create the most peaceful and relaxing environment possible.
During the course, the player finds cubes that must be dragged to the platform of the corresponding color, allowing a progress in the game.

- Limitations

As previously stated, the aim of this project was to create a virtual reality system for pediatric patients undergoing cancer treatments to be used as a pain distractor. Since this study's performance coincided with the pandemic due to Covid-19, we encountered some restrictions regarding carrying out user tests on patients undergoing pediatric cancer treatment, so this issue remains to be validated.

Ideally, children would have already experienced at least one chemotherapy session, and questionnaires would be taken to see how they felt during that period—analyzing the levels of stress and anxiety, as well as other complaints that could arise.
They would then be introduced to the game in virtual reality and explained what the game was about and how they could control their movements during the experience. Subsequently, an evaluation would be carried out to analyze how the use of VR contributes to the distraction of pain during treatment.
Through research, we also know that one of the side effects of treating this disease is nausea, so there is also a concern about not increasing this effect.

Also, time and several development limitations were factors that prevented the creation of a more extensive game, where it would be possible to validate whether this is really the way forward.

Nevertheless, one of the major limitations would be to have a large sample, in Portugal with the specific target audience, to test the system.

- Future work

The evaluation of the virtual reality system is a necessary part of the future work. User tests must be performed guided by the following criteria:
After analyzing the data of the ages with the highest incidence of pediatric cancer, it was concluded that this study should cover children aged 8-12 years. After selecting the age spectrum, tests should be performed on patients who have already had at least one chemotherapy session and whose consent of the doctor and caregiver is approved. Each test should have a maximum duration of 20 minutes and no gameplay instructions will be given, with the intention that the user can freely explore the scenario. After the stipulated time, an adequate questionnaire will be made to the user, where will be evaluated the gameplay, the level of immersion that the game provides, the quality of the experience and how effective with the pain distraction.
After performing the tests, an analysis of the virtual reality system must be performed in order to understand the strengths and the weaknesses of the work and how to improve it.

In conclusion, this is a system that needs validation with pediatric oncology patients in order to understand the potential of using a virtual reality system to be used during chemotherapy treatment.

Hopefully this study is a starting point for further investigation in this area.

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Appendix

Code used for the game.

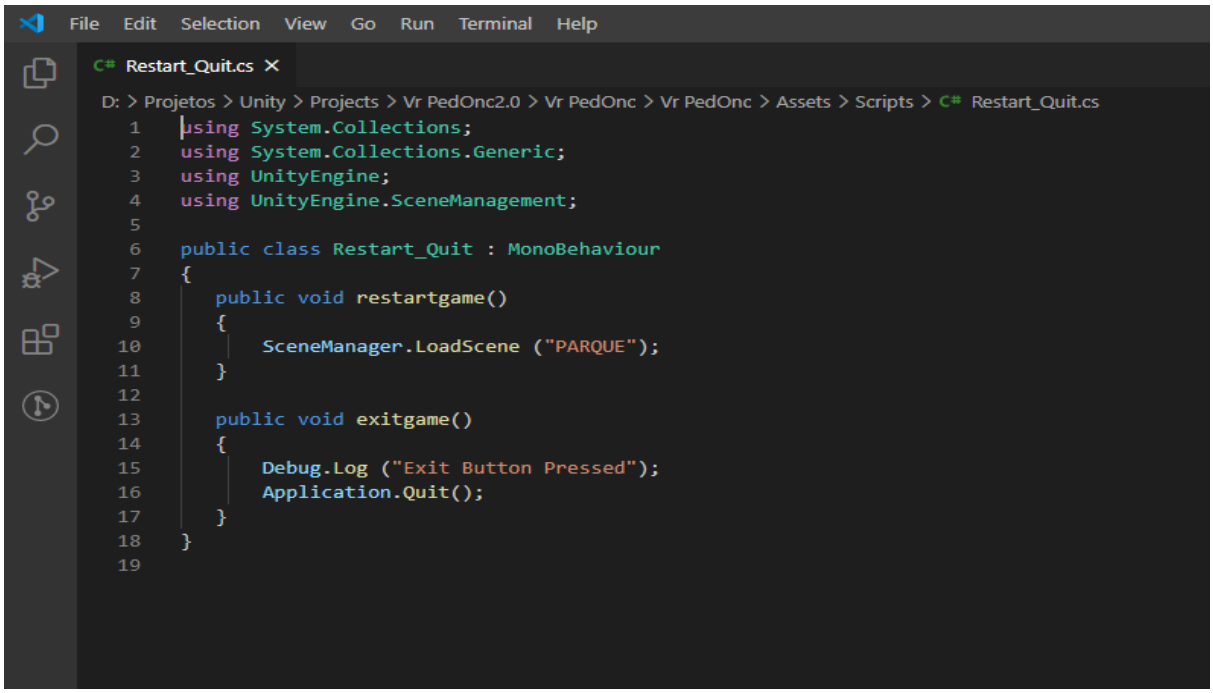

Figure a - Code of the start menu

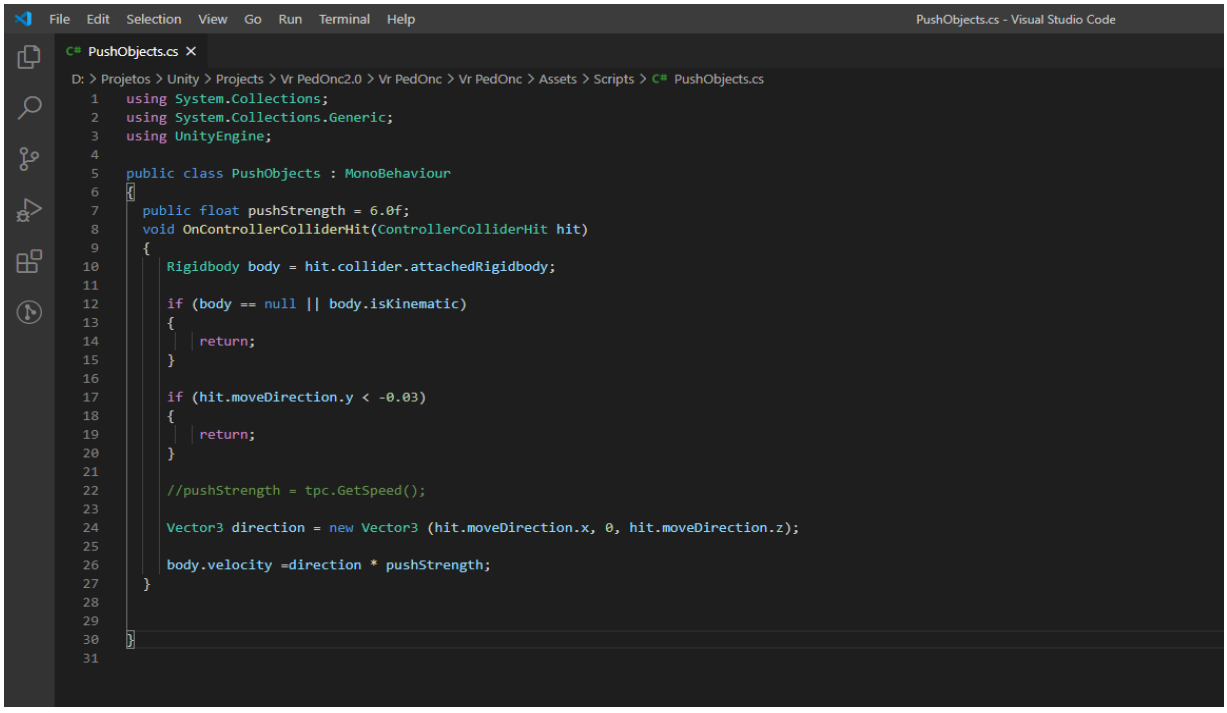

Figure b - Code used to make the character push objects

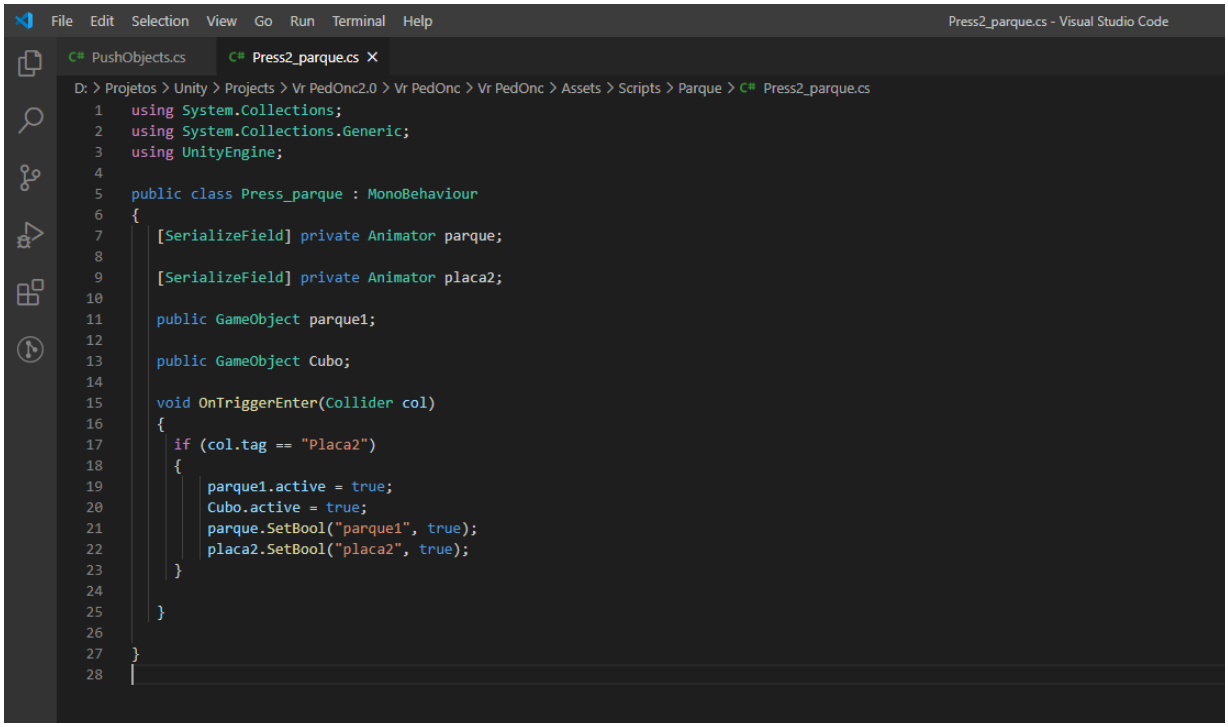

Figure c - Code for the interaction

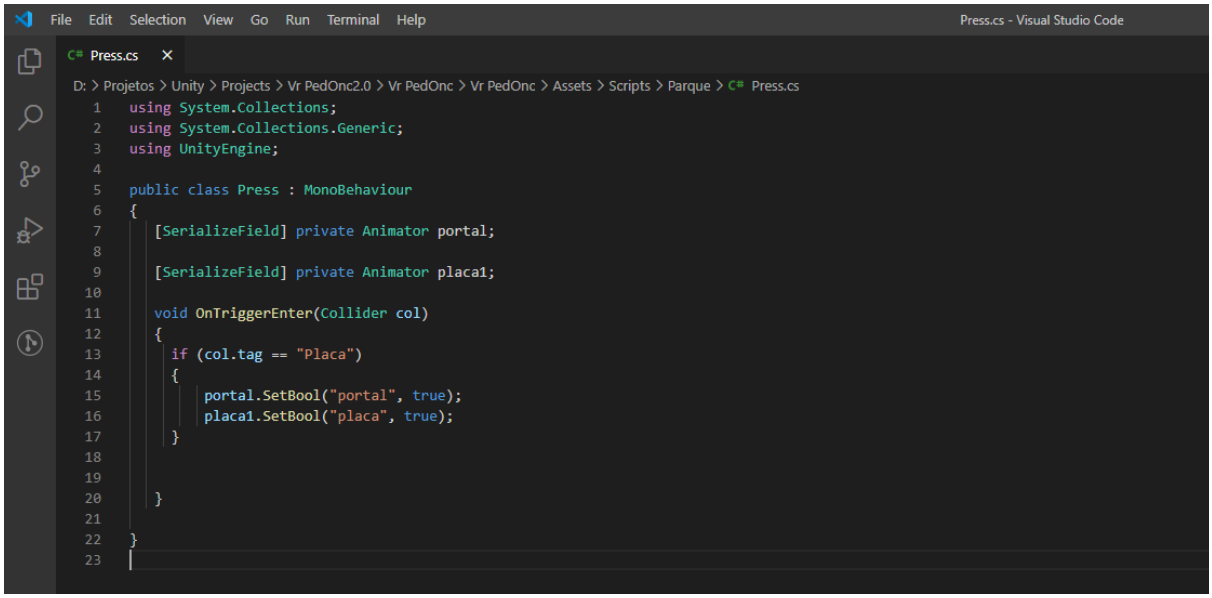

Figure d - Code with the cube that emerges after the first interaction.

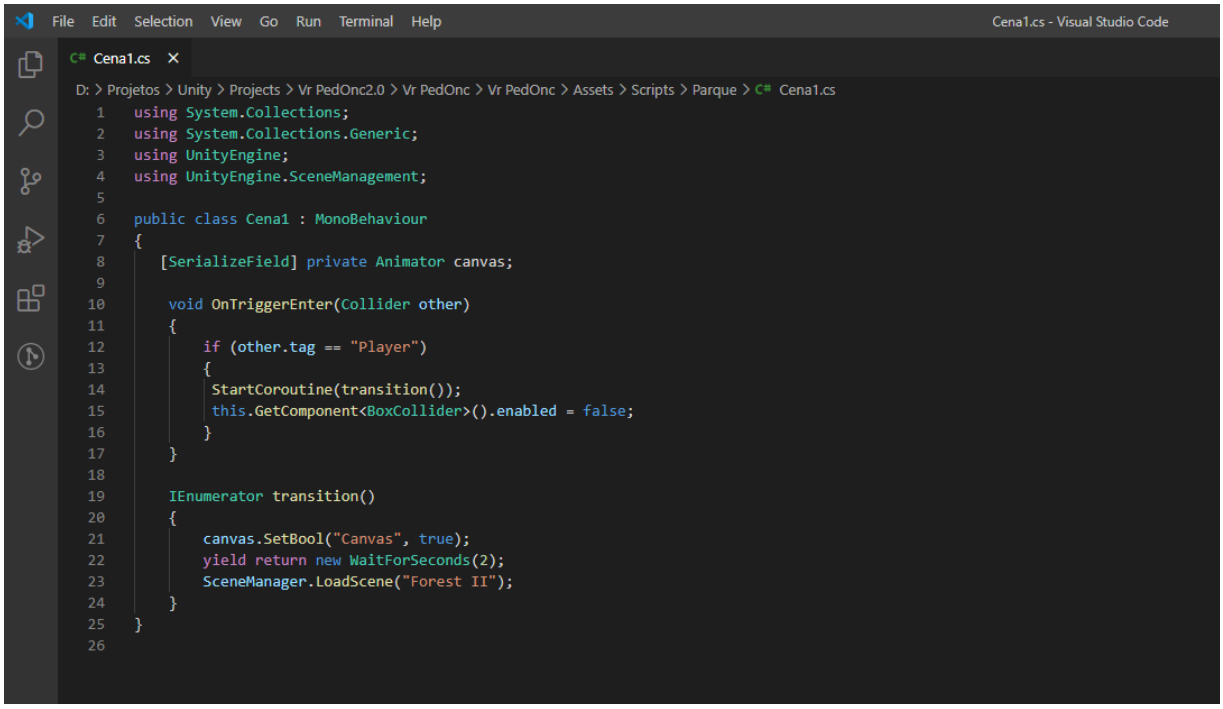

Figure e - Code used to change the scenario

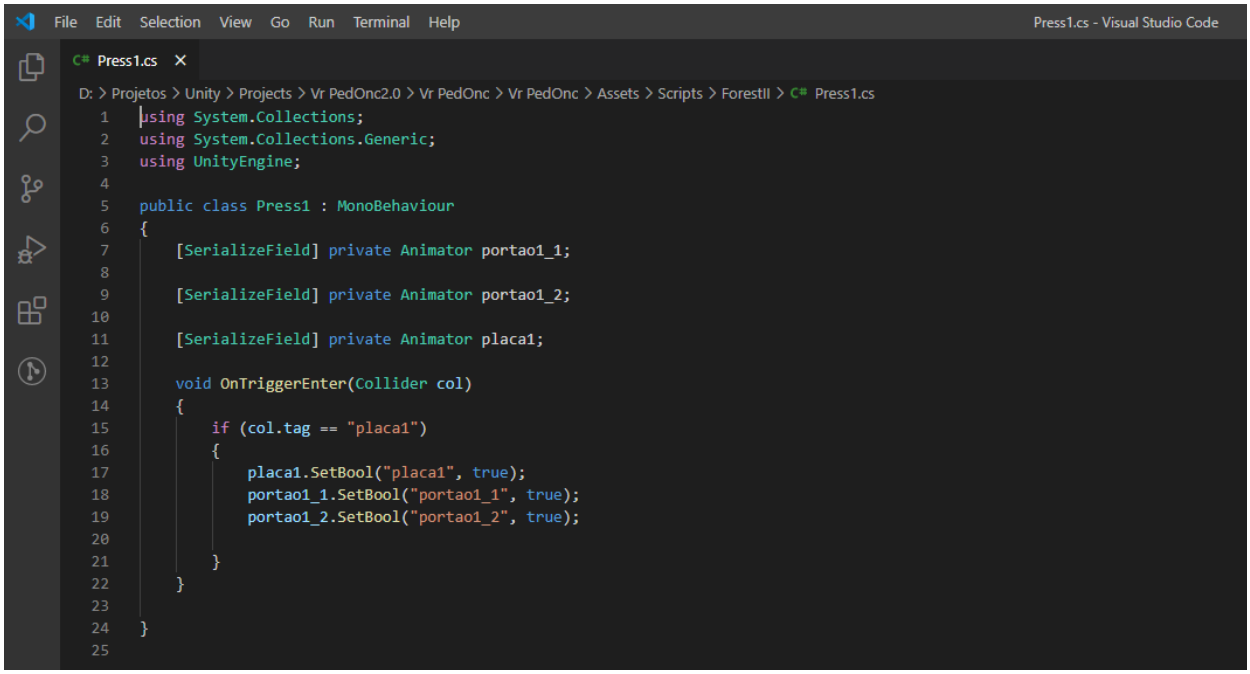

Figure f - Code for the interaction with the cube to open the door.

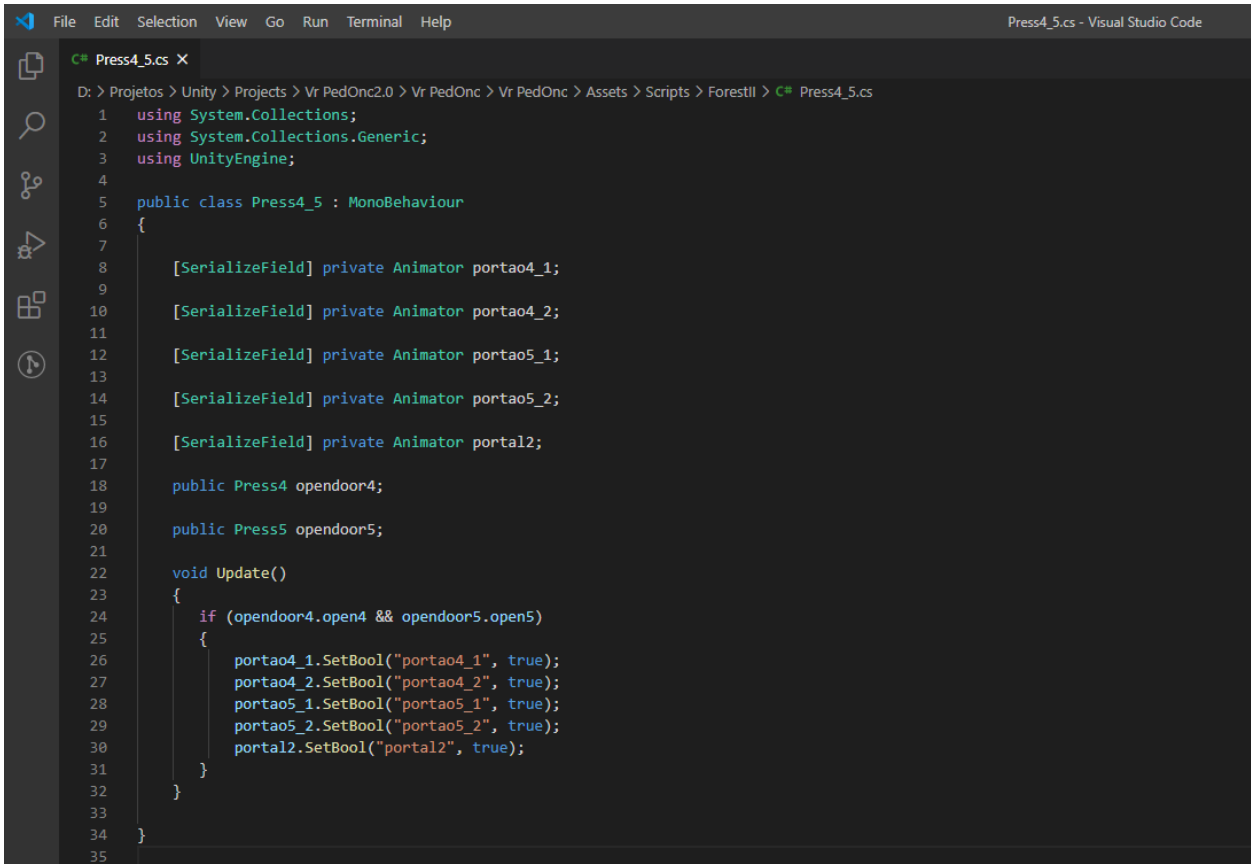

Figure g - Code for the new portal.

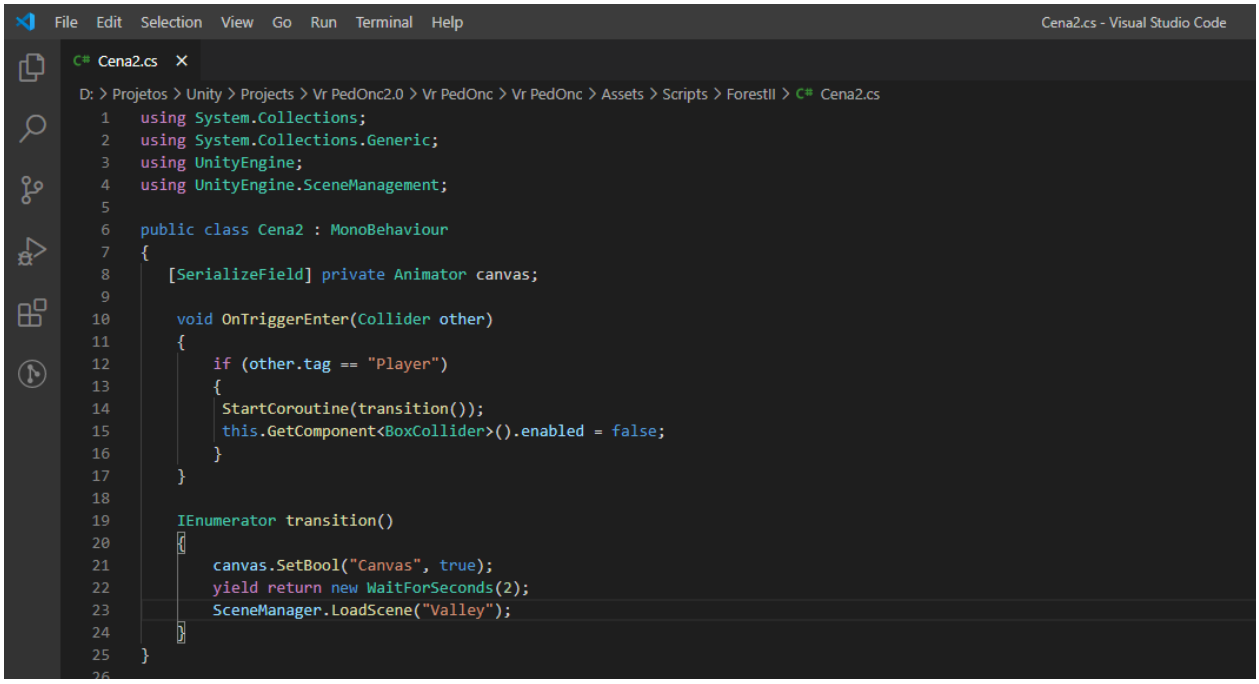

Figure h - The third scenario – Magic forest

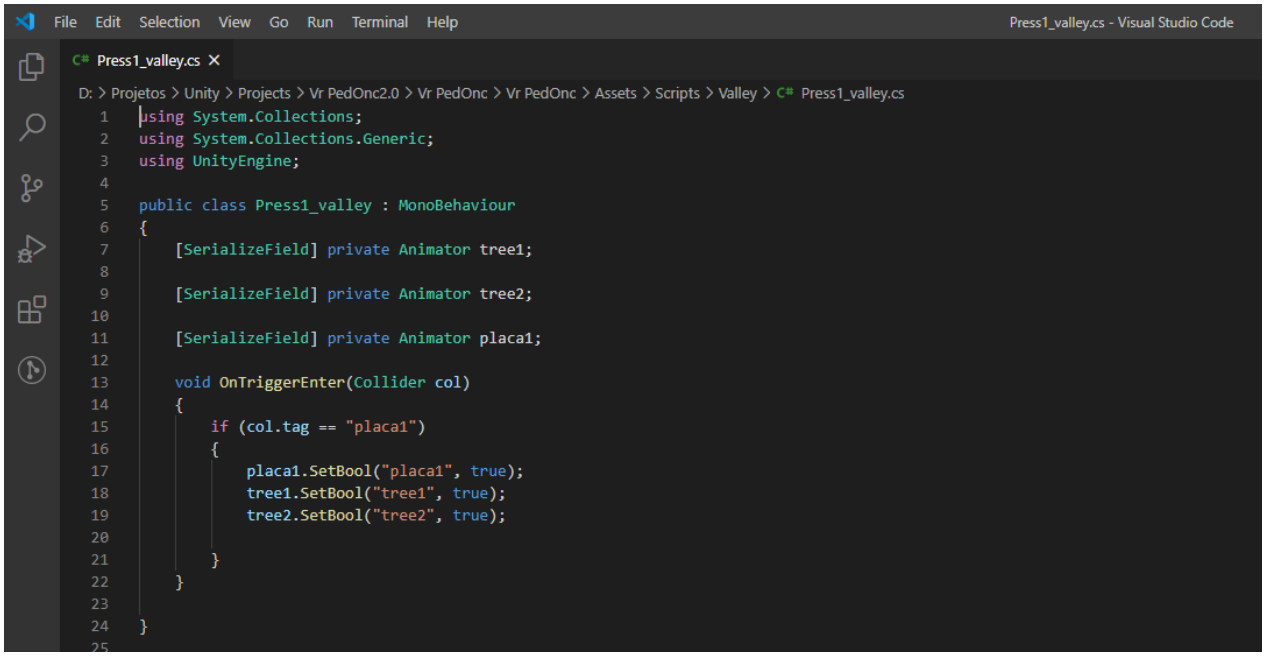

Figure i - Code used to change the scenario

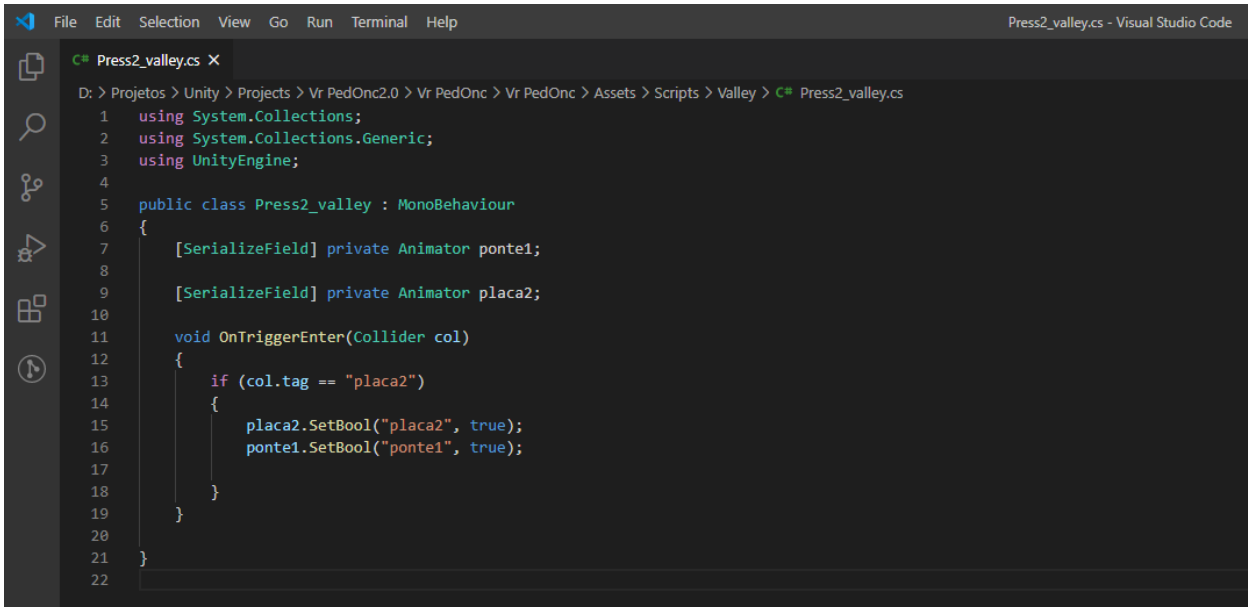

Figure j - Code used for the interaction

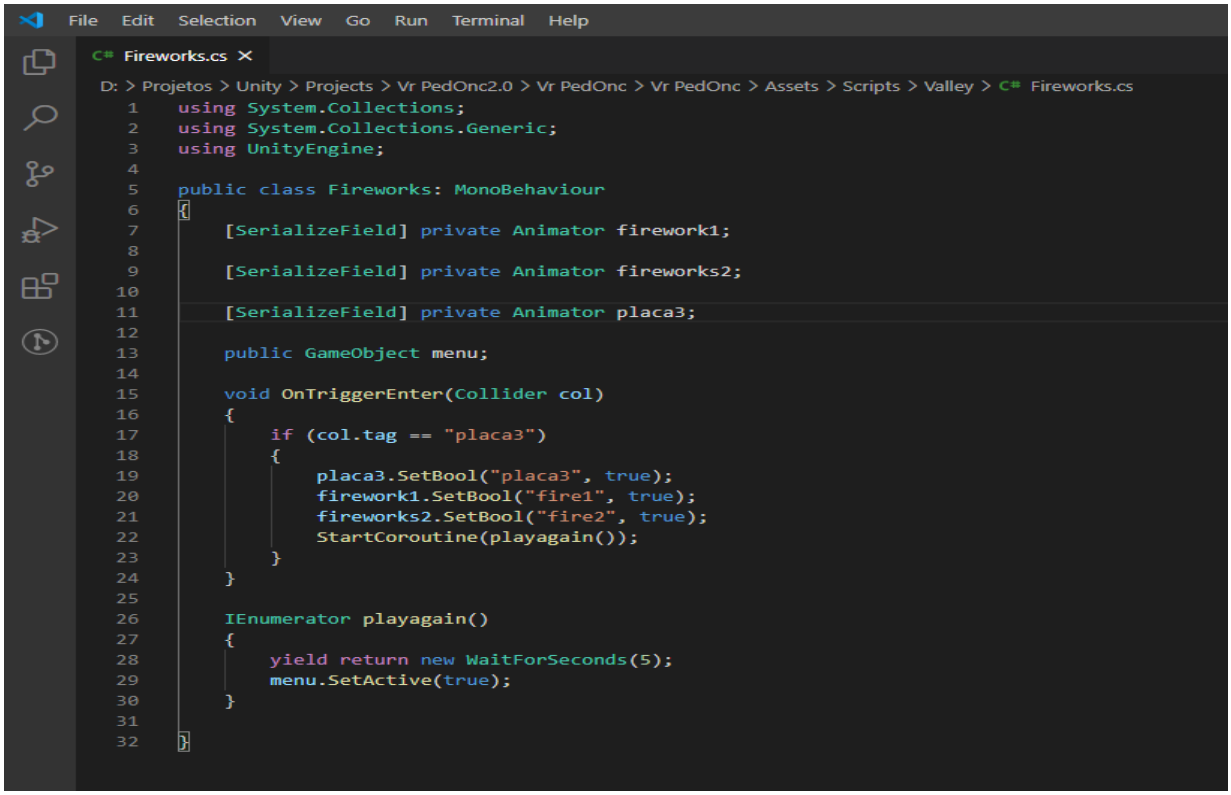

Figure k - Code for the menu