**INSTITUTO POLITÉCNICO DE LISBOA**

Instituto Superior de Engenharia de Lisboa
Escola Superior de Tecnologia da Saúde de Lisboa

# Effects of listening to music on patients who undergo bone scintigraphy

Maria Ferreira Boal

Trabalho Final de Mestrado para obtenção do grau de
Mestre em Engenharia Biomédica

Orientadores
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Tiago João Vieira Guerreiro (Faculdade de Ciências da Universidade de Lisboa)

janeiro de 2022

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# Resumo

**Definição do problema:** Segundo a Organização Mundial de Saúde o cancro é a doença mais incidente, no mundo no século XXI, e estima-se que este valor em 2050 aumente para 6,9 milhões de novos casos. Alguns dos fatores que levaram a esta crescente incidência de doenças oncológicas são o envelhecimento da população, aumento populacional, estilo de vida, alimentação, etc. A um diagnóstico de cancro estão associadas alterações físicas e emocionais nos pacientes, que podem provocar elevados distúrbios psicoemocionais. De entre os vários tipos de cancros, o da mama era em Portugal no ano de 2018, o terceiro mais incidente (12.0%) e o quinto em termos de mortalidade (6.0%). O cancro da mama é bastante comum em mulheres, mas não apresenta os mesmos sintomas ou gravidade nas doentes de igual forma. Esta doença maligna possui uma alta afinidade para metastização óssea, em cerca de 28-44% dos casos de cancro da mama este processo ocorre, apresentando-se com sintomas como dor severa e incapacidade de movimento. Devido a esta alta taxa de metastização para o osso, um dos exames que estas pacientes mais vezes realizam no percurso da doença é a cintigrafia óssea. Este método de imagem apresenta-se com particular relevância na avaliação, estadiamento e seguimento de doentes com cancro da mama, estando bem estabelecido na avaliação da distribuição de formação óssea ativa no esqueleto, permitindo relacionar com doença benigna e/ou maligna. Embora este tipo de exames, atualmente, constituam uma quasi-rotina para estes pacientes, não são desprovidos de impacto psicológico nomeadamente ansiedade. A ansiedade em doentes oncológicos é bastante comum aquando do diagnóstico e no decorrer da doença. Esta ocorre muitas vezes relacionada às consequências da doença (dor, perda de vida social e emprego), mas também está ligada a técnicas de diagnóstico, quer pela preparação necessária para alguns destes exames (intervalos de espera; ter de beber muitos líquidos), bem como o procedimento (falta de familiaridade com o procedimento; desconforto), equipamento (o tamanho do equipamento; natureza confinada do procedimento de aquisição de imagens; ter de se deitar numa maca estreita durante longos períodos de tempo), o medo de exposição à radiação e em relação aos resultados dos exames. A ansiedade é um estado mental caracterizado por uma intensa sensação de tensão, preocupação ou apreensão, em relação a algo adverso que possa acontecer no futuro. Esta apresenta sintomas psicológicos (desconforto; irritabilidade; diminuição da perceção da autoeficácia) e indicadores fisiológicos (aumento da tensão arterial, aumento do número de batimentos cardíacos por minuto, alteração da frequência respiratória, alteração do nível de oxigénio medido no sangue e inquietação ou nervosismo). A inquietação ou nervosismo, por si pode levar ao movimento do paciente durante a aquisição de imagens. Este movimento por parte do paciente resulta no artefacto de movimento, que afeta a leitura correta do exame bem como aumenta os custos associados e a exposição à radiação. Assim, várias estratégias têm sido aplicadas em diversos serviços de radiologia e medicina nuclear de forma a reduzir a ansiedade dos pacientes. Exemplos de algumas estratégias são informação escrita ou verbal antes de o paciente ver o equipamento, imaginário audiovisual, arteterapia, massagem terapêutica, relaxamento muscular progressivo, meditação, usar música calma e relaxante, etc. Sendo a abordagem mais utilizada a de ouvir música, no entanto, na pesquisa literária realizada, não encontrámos estudos sobre os efeitos fisiológicos da audição de música em pacientes que realizam cintigrafia óssea. Assim, após um parecer favorável do Comité de Ética da Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa a presente dissertação visa estudar o impacto da audição de música durante a aquisição de imagens de cintigrafia óssea na ansiedade dos pacientes.

**Objetivo:** O objetivo do presente estudo consistiu em avaliar o impacto da audição de música sobre os parâmetros fisiológicos e psicológicos, em doentes com cancro da mama, durante a aquisição de imagens da cintigrafia óssea na redução da ansiedade dos pacientes e na promoção do bem-estar dos mesmos.

**Metodologia:** Estudo exploratório, quasi-experimental realizado no serviço de medicina nuclear, *NuclearMed*, no Hospital Particular de Almada com os seguintes critérios de inclusão a) indicação clínica para cintigrafia óssea, b) ter cancro da mama, c) ter mais de 40 anos, d) sexo feminino, e) ser capaz de escrever, falar e compreender o português, e f) ser capaz de comunicar. As pacientes que aceitaram participar no estudo, era-lhes atribuído um número por ordem ascendente de participação no estudo. Os números ímpares constituíam o Grupo de Controlo, que seguia o normal protocolo do serviço de medicina nuclear e os números pares o Grupo Experimental, que também seguia este mesmo protocolo, mas que ouvia música pré-selecionada através de auscultadores durante a aquisição de imagens. As pacientes ouviam a música instrumental *Weightless* by Marconi Union com 71 batidas por minuto através de auscultadores tocada a partir de um MP4. De forma a avaliar o efeito da audição de música na ansiedade, foram utilizadas medidas fisiológicas (pressão sanguínea, frequência cardíaca, frequência respiratória e saturação do oxigénio no sangue), questionários de autoavaliação *State-Trait Anxiety Inventory* e acelerómetros de pulso. Todas estas medidas, exceto o acelerómetro de pulso, foram obtidas pré-exame (antes da injeção do radiofármaco) e pós-exame (após a aquisição de imagens). Os dados dos acelerómetros de pulso, foram obtidos durante 4 dias antes do exame e no próprio dia do exame. As pacientes também completavam um questionário pré-exame que recolhia informações sociodemográficas, sobre a saúde e atividade física e um questionário pós-exame que questionava sobre o procedimento realizado. A amostra consistiu em 30 participantes com uma média de idades de 57,70±8.09 anos, divididas de igual forma pelos dois grupos. Em relação às qualificações académicas na amostra 56,7%, tinham o ensino secundário, 63,3% eram casadas e 63,3% tinha um emprego.

**Resultados:** Os resultados deste estudo mostraram que os valores de tensão arterial foram elevados antes e depois do exame e que as pontuações do *State-Trait Anxiety Inventory* diminuíram após o exame em ambos os grupos. Também foram encontradas diferenças estatisticamente significativas entre os grupos em relação à frequência cardíaca e à saturação de oxigénio no sangue. Além disso, com significado estatístico, foi descoberta uma forte correlação entre a tensão diastólica e os resultados do *State-Trait Anxiety Inventory* pré-exame para o grupo de controlo e uma correlação moderada entre os resultados do *State-Trait Anxiety Inventory* pós-exame e a frequência respiratória para o grupo experimental. Em relação aos dados obtidos através da análise dos acelerómetros, verificamos que na véspera do exame as participantes têm mais períodos de sono durante o dia e permanecem nestes períodos por um intervalo mais longo em comparação com os outros dias.

**Conclusão:** Em conclusão, as pontuações *State-Trait Anxiety Inventory* diminuíram em ambos os grupos após o exame, sugerindo que as pacientes se encontraram mais ansiosas antes da realização da cintigrafia óssea. Em síntese, a utilização da audição de música para reduzir a ansiedade dos pacientes durante as cintigrafias ósseas parece ser um bom método, considerando que as pacientes que relataram sentir-se ansiosas no grupo experimental, na sua maioria, afirmaram que a audição de música ajudou a reduzir a ansiedade e que as pontuações *State-Trait Anxiety Inventory* e a tensão arterial sistólica diminuíram após a intervenção.

**Palavras-chave:** Ansiedade, Música, Cintigrafia Óssea, Cancro da mama

# Abstract

**Problem definition**: One of the most relevant oncology diseases is breast cancer, with an incidence of 12.0% in Portugal in 2018. Breast Cancer has a high rate of bone metastasis, so patients undergo bone scintigraphy for the detection of bone metastases due to its high sensitivity. Although this exam is almost routine for these patients, they still feel anxiety when they undergo it. There are many methods of reducing anxiety described in the literature, the most studied being listening to music. To our best knowledge, a study assessing whether listening to music contributes to anxiety reduction in patients undergoing bone scintigraphy has not yet been carried out.

**Aim:** This study aims to evaluate the effect of listening to music during bone scintigraphy on the level of anxiety in patients with breast cancer.

**Methodologies:** Exploratory, quasi-experimental study where 15 participants were included in the control group and 15 in the experimental group. Both underwent bone scintigraphy. The patients included in the experimental group listened to music during the image acquisition while the ones included in the control group did not. All patients answered to the pre-exam and post-exam questionnaires, as well as the State-Trait Anxiety Inventory questionnaire before scan and after scan, and physiological measures were also measured pre-exam and post-exam. Wrist accelerometers were used four days before the exam.

**Results:** Our results show that blood pressure values were elevated pre- and post-exam and that STAI scores decreased after the exam in both groups. We also established statistically significant differences post-exam between the groups in relation to heart rate and oxygen saturation in the blood. Additionally, with statistical significance, a strong correlation between STAI pre-scan and diastolic blood pressure for the control group, and a moderate correlation between STAI post-scan and respiratory rate for the experimental group were discovered. Furthermore, we found that the day before the exam participants have more sleepy periods during the day and stay in these periods for a longer duration compared with the other days.

**Conclusion:** In conclusion, listening to music to reduce patients' anxiety during bone scans seems to be a good method, considering that patients who reported feeling anxious in the experimental group, mostly stated that listening to music helped reduce anxiety and that STAI scores and systolic blood pressure decreased after the intervention.

**Keywords**: Anxiety, Music, Bone scintigraphy, Breast cancer

# Communications

Part of this dissertation resulted in a communication:

1. Oral, in SYMCOMP 2021, on the 25th of May 2021, Évora:

   a. Boal M, Pereira E, Vieira L. Different methods for measuring anxiety in patients undergoing bone scintigraphy. SYMCOMP 2021, on May 25, 2021, Évora.

2. Poster, at the 34th Congress of the European Association of Nuclear Medicine (EANM'21), 20-23 October 2021 (Online). The abstract is published in the European Journal of Nuclear Medicine and Molecular Imaging (EJNMMI):

   a. Boal M, Pereira E, Branco D, Guerreiro T, Vieira L. Contribution of listening to music in reducing anxiety in bone scintigraphy. Eur J Nucl Med Mol Imaging 2021;48:S650. DOI: 10.1007/s00259-021-05547-1

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# List of Acronyms and Abbreviations

| | |
|---|---|
| **APA** | American Psychological Association |
| **BC** | Breast Cancer |
| **BP** | Blood Pressure |
| **BS** | Bone Scintigraphy/Bone scan |
| **CG** | Control Group |
| **CT** | Computerized Tomography |
| **DIP** | Diurnal Immobility Periods |
| **DJ** | Daily Jerk |
| **DPA** | Daily Physical Activity |
| **EDA** | Electrodermal Activity |
| **EG** | Experimental Group |
| **FDG** | Fluorodeoxyglucose (18F) |
| **HR** | Heart Rate |
| **HRV** | Heart Rate Variability |
| **IEPE** | Internal Electronic Piezoelectric |
| **IS** | Interdaily Stability |
| **IV** | Intradaily Variability. |
| **Max** | Maximum |
| **Min** | Minimum |
| **mmHg** | millimetres of mercury |
| **MRI** | Magnetic Resonance Imaging |
| **NM** | Nuclear Medicine |
| **NPA** | Night Physical Activity |
| **NTID** | Night-Time Immobility Duration |
| **NTMD** | Night-Time Mobility Duration |
| **NTMP** | Night-Time Mobility Periods |
| **PET** | Positron Emission Tomography |
| **PET/CT** | Positron Emission Tomography/Computerized Tomography |
| **RA** | Relative Amplitude |
| **RR** | Respiratory Rate |
| **SNS** | Sympathetic Nervous System |
| **SpO2** | Blood Oxygen Saturation |
| **WBBS** | Whole-Body Bone Scintigraphy |
| **WT** | Wear Time |

# 1. Introduction

Cancer is a disease with a great impact in the 21-century due to an increase in life expectancy, sedentary behaviour, and high-fat diets. One of the most relevant cancer types worldwide is breast cancer with an incidence of 12.0% in 2018 (World Health Organization, **2020a**). This type of cancer has a high likelihood of metastasizing to the bone tissue, indeed this process occurs in 28-44% of patients (Glendenning & Cook, **2013**). This type of metastasis is usually diagnosed by bone scintigraphy.

Bone scintigraphy/bone scan (BS) is a highly sensitive and minimally invasive nuclear medicine imaging technique, that uses radiopharmaceuticals to observe bone metabolism or bone remodelling. Hence, it allows for the identification of various pathologies, namely bone metastases, sites of infection, fractures, and other bone lesions (Van den Wyngaert *et al.*, **2016**). This technique is used for diagnosing, staging, and monitoring disease, being the primary method for diagnosing bone metastases. In breast cancer, it is particularly relevant in the evaluation, staging, and follow-up of patients as it allows the observation of changes in the behaviour of metastatic lesions in response to treatments. Although these examinations currently constitute a quasi-routine for these patients, they are not devoid of psychological impact.

Anxiety in cancer patients is quite common at the time of diagnosis and during the disease. It is often related to the consequences of the disease (pain, loss of social life, and unemployment), but it is also linked to the diagnostic techniques, either by its procedure (lack of knowledge of the procedure, injection of the radiopharmaceutical, to name a few) or by the result of the examination (Abreu *et al.*, **2017**). Anxiety is an emotional response to stress, which may be accompanied by physiological stress indicators, such as an increase in blood pressure, increase in the heart rate, change in respiratory rate, change in the level of oxygen measured in the blood, increase in the amount of sweat produced in the feet and hands and restlessness or nervousness, which may lead to movement of the patient during the acquisition of images, resulting in motion artifact which affects the correct reading of the exam (de Witte *et al.*, **2020**; Grilo *et al*., **2020**; Van den Wyngaert *et al.*, **2016**).

Currently, there are several strategies aimed at reducing anxiety, among them: (a) being given written or verbal information before the patient sees the equipment (Leckie, **1994**); (b) audio visual images during the capture phase before images are obtained (Vogel *et al.*, **2012**), and (c) using music (de Witte *et al.*, **2020**; Lieber *et al.*, **2019**). Of these strategies, the most highlighted in the consulted literature was music to reduce anxiety in patients who underwent magnetic resonance imaging exams, angiography, Positron Emission Tomography/Computed Tomography, to name a few. In these studies, it was demonstrated that listening to music / making music/singing, leads to a decrease in heart rate (de Witte *et al*., **2020**). However, in the literary research carried out, we did not find studies on the physiological effects of listening to music in patients who perform bone scintigraphy. Thus, the present dissertation aims to study the effect of listening to music on the physiological parameters, in patients with breast cancer, during the imaging acquisition of bone scintigraphy. Another goal of this study is to analyse whether state anxiety affects the mobility of patients. Several studies have been carried out in order to assess whether the physical capacity of the patient is affected by depression or anxiety disorders. In these studies, it is concluded that patients with these diseases have lower levels of physical capacity (Chung *et al.*, **2020**), but most of these articles evaluate this correlation by self-completion questionnaires. Thus, it becomes important to objectively assess whether the state of anxiety also affects mobility. To this end, we will use a wrist accelerometer, a device that measures physical activity, and which is the most widely used method in assessments of physical activity in population studies (Doherty, Jackson, Hammerla, Plötz, *et al.*, **2017**). This method has shown good results in terms of validity for measuring physical activity in patients with schizophrenia and depression (Brien *et al.*, **2017**; Schuch *et al*., **2018**) and has already been used in studies assessing physical activity in patients with anxiety disorders (Dillon *et al.*, **2018**; Helgadóttir *et al.*, **2015**), but these articles do not report effects on the mobility of patients.

## 1.1. Objectives

The main objective of the study was to investigate the effect of listening to music on the physiological parameters, in patients with breast cancer, during the imaging acquisition of BS.

The secondary objectives are:

a) To evaluate the impact of listening to music during the acquisition of bone scintigraphy images on reducing anxiety in terms of patients' psychological parameters (State-Trait Anxiety Inventory).
b) To evaluate the impact of listening to music during bone scintigraphy imaging in reducing anxiety in terms of physiological parameters (blood pressure, heart rate, respiratory rate, and blood oxygen in blood) of the patients.
c) To assess whether state anxiety affects the mobility of bone scintigraphy subjects.
d) To verify the relationship between the two groups of patients who used different non-pharmacological strategies and the values of the psychological and physiological parameters obtained.

## 1.2. Dissertation Organisation

The dissertation is organised into six chapters. The first and current chapter, **Introduction**, describes the problem, the objectives that guided the research process, and presents the structure of the dissertation. The second chapter, **State-of-art**, contains a theoretical revision of the aspects that constitute the theoretical basis of this thesis. Thus, this chapter describes the epidemiology of cancer in particular breast cancer, the different imaging techniques for cancer diagnosis, the causes for anxiety in patients that undergo medical imaging, how anxious patients affect medical imaging, different strategies to reduce patient anxiety, how anxiety is measured and what are accelerometers and what they measure. The third chapter, **Methodologies**, describes the data set used, the instruments used for data collection, the ethical and legal procedures, selection of patients and music, the procedures before, during, and after BS, and statistical analysis. The fourth chapter, **Results**, presents the main results, obtained through data processing and statistical treatment. The fifth chapter, **Discussion**, discusses the results obtained. Finally, the last chapter, **Conclusion**, contains the conclusions, limitations and points out some perspectives for future works that may continue this line of investigation.

In relation to bibliographical referencing, the American Psychological Association (APA) Bibliographical Standard was used in this dissertation.

# 2. State-of-art

## 2.1. Oncologic diseases

Cancer is a public health problem worldwide and a leading cause of death in every country. The incidence and mortality of cancer is also rapidly growing worldwide each year, mainly due to an increase in life expectancy and changes in lifestyles (Bray *et al*., **2018**; Miranda *et al.*, **2015**; Miranda, N., Gonçalves, M. B., Andrade, C., Santos, **2018**).

Cancer can result from abnormal proliferation of the different types of cells in the body, so there are more than a hundred distinct types of cancer, which can vary substantially in their behaviour and response to treatment (Society, **2020**). The most prevalent types of cancer in the Portuguese population, estimated for 2020, were colorectum (17.4%), breast (11.6%), and prostate (11.2%) (World Health Organization, **2020b**). Previously in 2018**,** Figure 1, these had been the most incident with percentages of 17.6%, 12.0%, and 11.4% respectively (World Health Organization, **2020a**). Among men, the most prevalent type was prostate cancer (20.0%) and among women, it was breast cancer (26.4%) (World Health Organization, **2020b**).

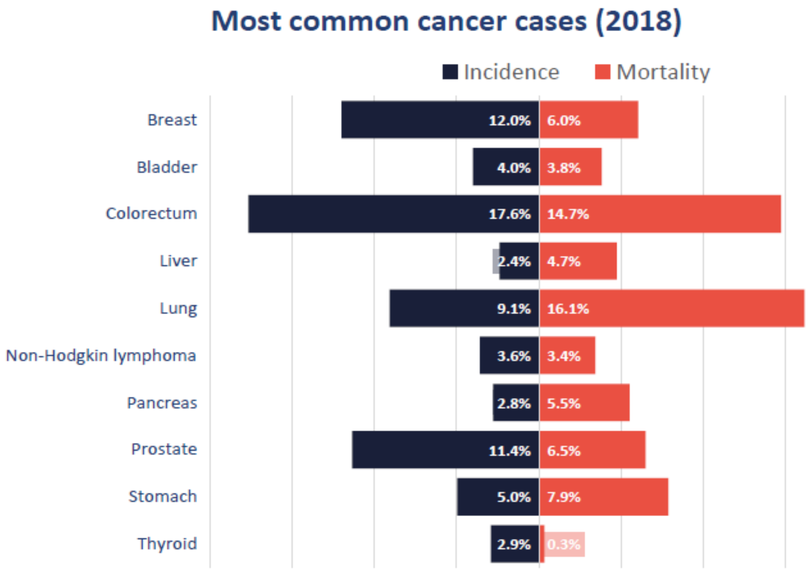


Figure 1- Most common cancer cases in 2018, in Portugal. Source: World Health Organization, (**2020a**).

With one million new cases of cancers reported in the world, breast cancer is common in females and comprises 18% of all women's cancer (Akram *et al.*, **2017**). In 2012, almost 1.7 million women were diagnosed worldwide and about half a million people died from this disease (Harbeck & Gnant, **2017**). In terms of breast cancer mortality, Portugal has one of the lowest mortality rates in the European Union (Miranda *et al*., **2015**).

Breast Cancer (BC) does not present in the same way in all women as it involves genetic and environmental factors (Barzaman *et al.*, **2020**). It can be classified into three groups taking into account molecular and histological evidence, **a)** BC expressing hormone receptor (oestrogen receptor or progesterone receptor), **b)** BC expressing human epidermal receptor 2, and **c)** triple-negative breast cancer (Barzaman *et al*., **2020**; Britt *et al*., **2020**). The BC expressing hormone receptor is the most common type (Barzaman *et al*., **2020**). Patients with primary or metastatic BC can be treated with chemotherapy, biological therapy, targeted therapy, hormone therapy, surgery, radiotherapy, or a combination of these treatments (Aktas *et al*., **2016**).

According to the anatomical localization, BC can be divided into two categories invasive and non-invasive. BC that has not extended away from the lobule or ducts where it is located, such as ductal carcinoma in situ and lobular carcinoma in situ are **non-invasive BC** (Akram *et al*., **2017**). On the other hand, tumours, where abnormal cells from within the milk lobules or ducts divide near the breast tissue are **invasive BC** (Akram *et al.*, **2017**).

The most common BC susceptibility genes are BRCA1 and BRCA2 (pathogenic mutations) (Britt *et al.*, **2020**). High and moderate BC predisposition genes are cadherin 1, PTEN, serine/threonine-protein kinase 11, TP53, checkpoint kinase 2, ataxia telangiectasia mutated, nibrin and partner and localizer of BRCA2 but germline mutations in all of these are rare (Britt *et al*., **2020**).

BC is also connected with non-genetic risk factors such as increased age, personal history of breast pathologies, premature menarche, late menopause, high mammographic density, use of oral contraceptives, menopausal hormone therapy, alcohol consumption, overweight and obesity, shorter breastfeeding periods, and a lack of physical activity (Britt *et al.*, **2020**).

Through monitoring patients with imaging techniques and/or the presentation of symptoms, such as breast pain or a palpable mass, breast cancer is diagnosed (Jafari *et al.*, **2018**). Some of those imaging techniques are breast ultrasound, mammography, magnetic resonance imaging (MRI), positron emission tomography (PET) scan, computerized tomography (CT) scan, and single-photon emission computed tomography (Akram *et al*., **2017**; Jafari *et al.*, **2018**). These have not only been used for diagnosis but also to monitor patients with BC in various stages. Of all these techniques, mammography and breast ultrasound are the gold standards for the detection of BC (Jafari *et al*., **2018**).

The most common site of BC to metastasize is the bone tissue, with this process occurring in 28-44% of patients (Glendenning & Cook, **2013**). Some of the most common symptoms of bone metastases are sudden severe pain and the inability to move and/or pain in the back or neck. The diagnosis of bone metastasis is usually obtained by imaging tests, such as bone scan, x-rays, CT scan, MRI, and PET scan (Iagaru & Minamimoto, **2018**).

According to literature, patients treated for cancer have a prevalence of major depression (15%), minor depression (20%), and anxiety (10%) (Pitman *et al.*, **2018**). Two-thirds of patients with cancer and depression also have clinically significant anxiety symptoms. In BC 9.0% suffer from major depression (Pitman *et al.*, **2018**). Some causes that lead to these mental disorders are mostly the patient's psychological reactions to diagnosis, treatment, relapse, end-of-life care, or survivorship (Pitman *et al.*, **2018**).

### 2.1.2. Imaging techniques for cancer diagnosis

Common imaging tests for cancer diagnosis include CT scan, MRI, X-ray, PET scan, and bone scan/ bone scintigraphy (BS) among others. These imaging exams allow doctors to examine bones and internal organs in a non-invasive way.

An X-ray is a common imaging test used by doctors to diagnose, monitor, and plan treatments for many conditions, including some cancers (e.g., bone, lungs, stomach, kidneys, or breast cancer). A digital imaging technique that also uses X-rays is the CT scan. This technique uses special X-ray equipment with computing algorithms to create cross-sectional digital images, in order to differentiate tissues and structures within the patient body (Badnjevi & Pokvić, **2020**; Nieman *et al.*, **2015**; Seeram, **2010**).

Two additional imaging tests used in the oncologic setting are MRI and PET. An MRI is the best imaging modality for soft tissue contrast (Badnjevi & Pokvić, **2020**; Pomerantz, **2020**). However, the equipment is high cost, image acquisition takes lengthy periods, is noisy, has a narrow space structure for the scan, and is sensitive to patient movement (Badnjevi & Pokvić, **2020**; Pomerantz, **2020**). The PET scan uses a glucose analogue, [$^{18}$F]fluorodeoxyglucose (FDG) that accumulates in metabolically active tissues, such as tumours that have an overexpression of membrane transport proteins (Pomerantz, **2020**). This imaging modality is the imaging standard for cancer diagnosis, while whole-body bone scintigraphy (WBBS) is commonly used to detect bone metastases because of its high sensitivity, ability to image the entire skeleton, low cost, and is widely available (Gnanasegaran *et al.*, **2009**; Iagaru & Minamimoto, **2018**; Love *et al.*, **2003**).

The scan we focus on in this study, WBBS, is performed with technetium-99m–labelled diphosphonates that rapidly accumulate in the bone tissue, in 2–6 hours after the radiopharmaceutical injection, about 50% of the injected dose has been accumulated in the skeletal system (Love *et al*., **2003**) enabling the acquisition of images in the gamma camera. Clinical indications for skeletal scintigraphy include detection, evaluation, and/or follow-up of metastatic bone neoplasms, primary benign and malignant bone neoplasms (American College of Radiology, **2017**). To carry out this exam it is not necessary to comply with a period of fasting. The procedure of WBBS starts with the intravenous injection of $^{99m}$Tc-diphosfonate (e.g., $^{99m}$Tc-HMDP), after the injection patients must wait for 2 to 4 h before entering de gamma camera. In this period patients are encouraged to increase hydration and to void as frequently as possible. Before entering the gamma camera, patients are instructed to void one last time. The image acquisition length is approximately 20 minutes.

## 2.2. Anxiety and the causes in patients

Anxiety is a psychological and physiological state characterized by cognitive, physiological, and behavioural components. It is described as a mental state characterized by an intense sense of tension, worry, or apprehension, relative to something adverse that might happen in the future (Saviola *et al.*, **2020**). Researchers distinguish aspects of anxiety into **state**, defined as a more transient reaction at a given moment in time, and **trait**, described as a more stable personality attribute in experiencing events with an excessive degree of anxiety over a long period (Major *et al.*, **2000**; Martinez Lorca *et al.*, **2017**). Moreover, state anxiety is brief and short-lived, this can be exhibited by a person experiencing a medical procedure, such as an imaging exam or blood test (Wilson *et al.*, **2013**). On the other hand, trait anxiety is a more stable tendency to respond to a fright situation and it is more linked to the personality trait of neuroticism (Wilson *et al.*, **2013**).

It is a state of apprehension that has psychological and somatic symptoms, due to an increase in the activity of the autonomic system specifically the activation of the sympathetic nervous system (SNS). Psychological symptoms are feeling of tension, worry, fear, restlessness, and difficulty in concentrating (Lo Re *et al*., **2016**; Major *et al.*, **2000**). Somatic symptoms cause hyperactivation of the central nervous system, causing motor restlessness, tremors, headache, sleep disturbances, autonomic symptoms (sweating, hot flashes or chills), dry mouth, dizziness palpitations, paraesthesia, thoracic pain and dyspnoea, urinary urgency, and gastrointestinal symptoms, increased heart rate, blood pressure, and respiration rate (de Witte *et al.*, **2020**; Lo Re *et al*., **2016**; Major *et al*., **2000**).

In the literature, we find several causes of patient anxiety, we can divide them into four categories **diagnostics** (e.g. due to diagnosis and treatments and exams results), **preparation and procedure** (e.g. previous negative imaging experiences; unfamiliarity of the procedure; waiting intervals; having to drink lots of liquids and discomfort), **equipment** (e.g. the size of the equipment, particularly in claustrophobic patients; confined nature of the acquisition procedure; having to lie on a narrow stretcher for long periods of time and possible positioning discomfort), and **radiation** (e.g. injection of radiopharmaceuticals and fear of radiation exposure) (Abreu *et al*., **2017**; Grilo *et al*., **2020**; Leckie, **1994**; Shortman *et al*., **2015**).

Some major concerns for patients are claustrophobia and radiation effects. Claustrophobia showed incidences of up to 65% in MRI- associated anxiety (Heyer *et al.*, **2015),** and 54.5% of the patients that searched for information before positron emission tomography/computerized tomography (PET/CT), reported radiation effects as the main predisposing concern factor (Abreu *et al.*, **2017**). Raised anxiety levels were associated with an imaging modality, medical condition, first time having the procedure, lower patient-perceived health status, and the female gender (Forshaw *et al*., **2018**). In Abreu *et al*. (**2017**) and Forshaw *et al*. (**2018**), it was concluded that women were more anxious in comparison to men when undergoing different imaging modalities.

A comparison of cancer patient experience between $^{99m}$Tc-HDP BS and $^{18}$F-FDG PET/CT revealed that the patients that underwent a BS were more anxious than the PET/CT group (Grilo *et al.*, **2020**). It also revealed that exam duration was the main trigger of anxiety in patients who undertook a BS, while in the PET/CT group the main concern was the exam result (Grilo *et al.*, **2020**).

### 2.2.1. Patient anxiety affects medical imaging

Patient anxiety when undergoing a nuclear medicine (NM) procedure can be a real problem for technologists, as uncontrollable anxiety can affect imaging results. Thus, one of the tasks of NM staff is to make sure the patient is comfortable, relaxed, and collaborative (Acuff *et al.*, **2014**).

As mentioned previously anxiety is characterized by an increased autonomic system activity with an array of symptoms. Of these symptoms, motor restlessness and tremors are the bigger problems for imaging as they can result in motion artefact, which can cause longer procedural times or the need for repeated procedures (Abreu *et al.*, **2017**; Forshaw *et al.*, **2018**). In addition, anxiety can also cause discomfort affecting the normal biodistribution of $^{18}$F-FDG, leading to increase uptake in muscle or brown adipose tissue and reduced diagnostic quality of the images of the PET/CT (Abreu *et al.*, **2017**; Shortman *et al*., **2015**). Patient anxiety can also lead to imaging procedure cancellations and increased use of sedatives (Forshaw *et al*., **2018**). One study found that 72.0% of radiographers reported that anxiety was an issue for patients before undergoing MRI, and that 19.3% reported that anxiety impacts scanning regularly (Forshaw *et al.*, **2018**).

All these problems have adverse implications for the health care system, for example, anxiety-associated cancelling of MRI is estimated to cause a loss of productivity of approximately 1 billion Euros (Heyer *et al.*, **2015**).

### 2.2.2. Strategies to reduce patient anxiety

Patients that undergo a medical procedure often experience anxiety which can be aggravated by a hospital setting. As mentioned earlier anxious patients can affect an imaging result by moving, which leads to reduced image quality, increases health care costs, and increased exposure to radiation (Munn & Jordan, **2014**). Also, anxiety can decrease patient comfort which results in lowered compliance and decreased satisfaction with the hospital experience. To reduce anxiety technologists can resource to pharmacologist or non-pharmacologist strategies. Some medications such as anxiolytics and anxiety-reducing drugs can reduce pre-procedural anxiety in patients waiting for a medical exam, however, the scientific community has no consensus on the benefits (King *et al.*, **2021)**. Some disadvantages this strategy has are waiting for the medication to take effect, associated costs, ethical objections, the inability of outpatients to drive afterward, and adverse reactions to other drugs (Forbes *et al.*, **2020**; King *et al.*, **2021**; Vogel *et al.*, **2012**). As a result of the disadvantages of pharmacology, researchers have tried to find non-pharmacological strategies to reduce anxiety.

In the literature, the non-pharmacological strategies that contribute most to reducing anxiety are audio-visual imagery, music, physical exercises, art therapy, massage therapy, mental distraction, meditation, progressive muscle relaxation, breathing exercises, Reiki, and better communication (Dib *et al.*, **2020**; Leckie, **1994**; Lorca *et al.*, **2019**; Martinez Lorca *et al.*, **2017**; Philips Healthcare, **2013**; Törnqvist *et al.*, **2006**; Vogel *et al.*, **2012)**.

Audio-visual imagery occurs in the uptake room or waiting room where a television, headphones, lights, backlit nature images/photographs, or the Philips Ambient Experience uptake room, Figure 2, is present (Philips Healthcare, **2013**; Stanley *et al.*, **2016**; Vogel *et al.*, **2012**). Frequently videos are passed on the television, these videos can be of natural landscapes accompanied by nature sounds or music such as relaxing music or videos recorded by the NM staff explaining the procedure or showing the procedure that follows (Sun *et al.*, **2020**; Vogel *et al.*, **2012**). The Philips Ambient Experience uptake room has a ceiling unit that generates procedure-specific audiovisual scenarios, that include practical procedural lighting and audio settings (Philips Healthcare, **2013**). Different colour settings and sounds are used through the injection procedure and uptake phase until is time for the exam. This strategy of audio-visual imagery can happen during the exam for example in the MRI by placing a monitor at the backside of the scanner and using a mirror to redirect the image to the patient's eyes, therefore allowing the patient to watch what's on the screen while lying in the scanner (Philips, **2016**).

Figure 2- Philips Ambient Experience uptake room solution. Source: Philips Healthcare, **2013**.

With the effect of reducing patient anxiety, many studies have evaluated the effects of written and verbal information, extended written information, immediate interpretation of results, and assessed which of the formats, written, visual or verbal, is better for decreasing anxiety (Kemp *et al*., **2020**; Leckie, **1994**; Törnqvist *et al.*, **2006**; Yakar & Pirinçci, **2020)**. In the case of a BS explaining what radiopharmaceuticals are, how they work, the duration of the exam, why does the patient have to wait an hour and a half after injection to undergo the exam, to name a few. Visual communication is very similar to written and verbal, that is, it gives the same information but in a video form. In a study by Yakar & Pirinçci (**2020**), it was found that visual information is more successful in reducing anxiety before MRI than written information. A different way of bettering communication is using tangible devices, for example, a standard wireless doorbell or a squeeze bulb, Figure 3. These devices allow the patient to feel a physical connection to the technologist being reassured that if a problem happens they can reach for help (Acuff *et al.*, **2014**). An interesting finding in Acuff *et al.* (**2014**) study was that the type of communication device does not matter so much as making patients aware that they can easily contact the imaging staff during their procedure.

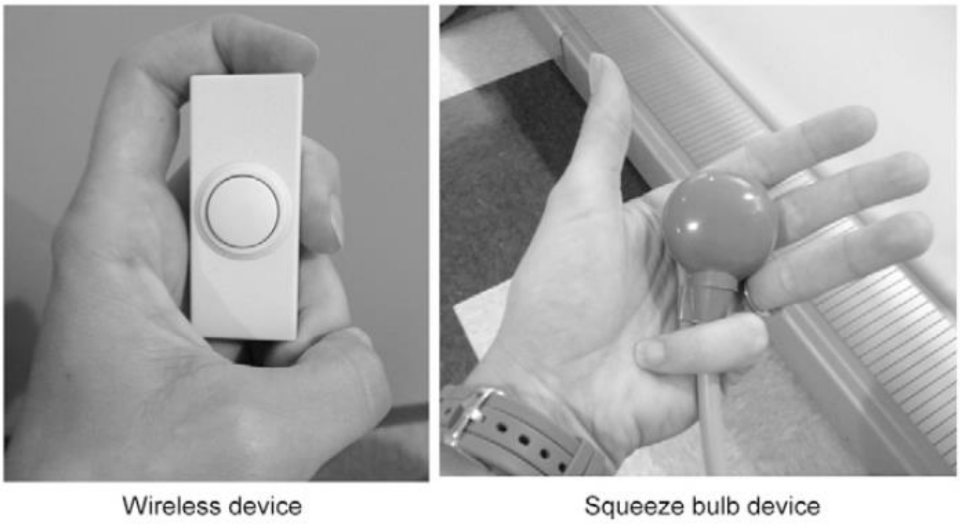


Figure 3- Tangible objects use in Acuff *et al*. (**2014**) Wireless doorbell (left) and squeeze bulb (right). Source: Acuff *et al*. (**2014**).

Some physical exercises such as aerobic fitness, flexibility, and muscle strength, in home settings, self-managed patient programs, and individual and group sessions have been specifically studied to observe their effects on anxiety. The results obtained were mixed, some studies suggested a significant improvement and others showed no significant improvement (Smith *et al*., **2015**). However, exercise interventions were found to improve quality of life (Smith *et al.*, **2015**). In the case of aerobic exercise, a reduction in anxiety symptoms or a reduction in anxiety sensitivity was observed (Stonerock *et al*., **2015**).

Art therapy includes painting, sculpting, poetry, and drama (Smith *et al.*, **2015**; Tang *et al*., **2019**). Painting therapy can pass by talking about the materials, the different techniques of painting, and the drawing technique (Bosman *et al*., **2021**). The literature suggests that art therapy benefits female breast cancer patients with respect to the treatment of anxiety, depression, and fatigue. Nevertheless, additional studies are needed as sample sizes tend to be small (Smith *et al.*, **2015**; Tang *et al*., **2019**).

Reiki consists of the laying on of hands for the transfer of energy. A study administering Reiki to women with various types and stages of cancer reported a significant reduction in anxiety (Smith *et al*., **2015**).

Progressive muscle relaxation training and practice in relaxing each muscle group were found to decrease anxiety as patients monitored tension in specific body muscle groups, deliberately inducing and relaxing tension in each (Smith *et al.*, **2015**).

Mindfulness is defined as paying attention in a particular way, on purpose, in the present moment, and non-judgmentally (Xunlin *et al*., **2020**). Interventions based on mindfulness allow individuals to maintain an appreciation of the present moment, disengage themselves from unhealthy beliefs, thoughts, or emotions, and heighten their sense of emotional balance and well-being (Xunlin *et al.*, **2020**). This strategy allows for the acceptance of the cancer diagnosis, clarifying individuals' values, and committing to actions that enrich their lives (Xunlin *et al.*, **2020**).

Among all these strategies, the most highlighted in the consulted literature was music to reduce anxiety in patients who underwent MRI, angiography, PET/CT, to name a few. In these studies, it was demonstrated that listening to music/performing music/singing, leads to a decrease in heart rate (de Witte *et al.*, **2020**). This approach can be executed in different ways in some studies the music that the patient listens to is selected by them, in other studies, the patients select the music that they want to hear from a playlist set by the investigators, and in other studies, the music is pre-selected by the investigators (Chen *et al.*, **2013**; de Witte *et al.*, **2020**; Dib *et al.*, **2020**; Lee *et al.*, **2017**; Mohammadi *et al.*, **2014**). Pre-select music is the most used as it gives the investigators the control of choosing music with certain characteristics. In a systematic review by de Witte *et al.*, (**2020**), the authors concluded that instrumental music shows better results in reducing anxiety than music with lyrics and that music with a slower tempo, 60-80 beats per minute is one of the characteristics that have more effect in the reduction of patient anxiety, leading to a reduction in heart rate. Music intervention helps to reduce anxiety, cope with physical problems, improve quality of sleep and relieve the emotions caused by cancer (Mohammadi *et al.*, **2014**). As such it can be an important care tool, free of side effects, easily available, and associated with a low financial burden.

In this study, we focus on the strategy of listening to music as a way of reducing anxiety in patients undergoing BS, as it is the most used method, even though to our knowledge it has not been used in BS exams to reduce patient anxiety.

## 2.3. Measures of Anxiety

Anxiety is an emotion that can be experienced acutely and briefly or represent a more stable and enduring underlying personality trait. It has many dimensions, such as emotional, cognitive, behavioural, and somatic. Being characterized by a heightened autonomic system activity particularly the activation of the SNS (Major et al., **2000**; Wilson et al., **2013**). Anxiety has psychological symptoms such as feelings of apprehension, distraction, procrastination, avoidance, compulsions, light-headedness, and physically symptoms such as increased heart rate, blood pressure, and respiration rate, sweating, dizziness, and trembling motor tension such as fidgeting or muscle tension (de Witte *et al.*, **2020**; Dib *et al.*, **2020**; Guinot Jimeno *et al.*, **2011**; Major *et al.*, **2000**; Wilson *et al.*, **2013**). Therefore, anxiety can be measured with psychology measurements (self-report measures), physiological measures (e.g., heart rate, blood pressure, muscle tone, respiration rate), biochemical parameters (e.g., cortisol levels), and behavioural measures (e.g., speech dysfluencies, bodily movement, handwringing).

### 2.3.1. Psychological parameters

Self-report measures can be divided into three categories: **(a)** measures of trait anxiety, **(b)** measures of state anxiety, and **(c)** measures of situation-specific anxiety, such as test anxiety. In this study, we focus on measures of state anxiety.

Measures of state anxiety are self-report or administered by a health professional. The state anxiety measures include the Endler multidimensional anxiety scales (for age 12-adult), The State-Trait Anxiety Inventory (form y) for adults, and children (Wilson et al., 2013).

The Endler multidimensional anxiety scale is a self-report measure that has three forms, the Trait form, the State form, and the Perception of Situations form. We focus on the State form which consists of 20 items, ten of which measure the autonomic-emotional component of state anxiety and ten of which measure the cognitive worry component of state anxiety (Endler *et al*., **1989**). This scale is rated on a five-point, intensity scale ranging from (1) not at all to (5) very much.

The State-Trait Anxiety Inventory (STAI) for adults is the most widely used measure to assess this type of anxiety in the literature. The purpose of the STAI is to measure the presence and severity of current symptoms of anxiety and a generalized propensity to be anxious. This questionnaire has two subscales, first, the State Anxiety Scale evaluates the current state of anxiety by asking the person on a four-point scale (not at all, somewhat, moderately so, or very much so) how they feel right now. It does this by using items that measure subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system (Butcher *et al*., **1998**; Julian, **2011**). The other sub-scale, The Trait Anxiety Scale, evaluates relatively stable aspects of anxiety proneness with a four-point scale (almost never, sometimes, often, or almost always)(Butcher *et al.*, **1998**; Julian, **2011**). Since 1966 this questionnaire has been translated into over 48 different languages and used in a variety of clinical settings. The difference between STAI for adults and children resides in how they are administered. In the case of children, verbal administration is given by a health professional.

### 2.3.2. Physiological parameters

Comparing self-report, behavioural, and physiological measurements the latter are less easily controlled by the participant, thus providing a potentially more accurate assessment of anxiety. A brief description of the physiological parameters is given below.

**Blood Pressure (BP)** is the pressure of blood against the blood vessel walls during the cardiac cycle. Is measured in millimetres of mercury (mmHg) and is given in two numbers, systolic and diastolic pressure. It is measured by a blood pressure monitor. The American College of Cardiology in a 2017 guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults define normal BP level as less than 120/80 mmHg, elevated BP as between 120-129 mmHg for systolic pressure, and less than 80 mmHg for diastolic pressure, and high blood pressure as higher than 130/80 mmHg. Temporary increases in BP are an indication of the activation of the SNS. BP and anxiety levels are assumed to be positively correlated (Roos *et al.*, **2021**).

**Heart rate (HR)** is the number of heart beats per minute, and it is measured by checking the pulse. The normal resting heart rate is between 60 and 100 beats per minute. Is sometimes assumed to directly reflect anxious arousal (Roos *et al*., **2021**).

**Heart rate variability (HRV)** is a measure of the variation in time between each heartbeat. Is measured by the standard deviation of normal-to-normal N-N intervals. HRV is associated with perceived stress (Kim *et al.*, **2018**; Roos *et al*., **2021**). HRV is typically higher when the heart is beating slowly and decreases as the heart beats more quickly. That is, HR and HRV have a generally inverse relationship.

**Respiratory rate (RR)** is the number of breaths a person takes per minute. Changes in breathing can be the outcome of an increased level of anxiety or the source of threat experienced by the individual, which, in turn, leads to increased anxiety (Paulus, **2013**). The normal RR rate at rest for an adult is 12 to 20 breaths per minute. Anxiety and stress affect the RR which over time can alter oxygen saturation and/or carbon dioxide levels in the blood.

**Blood Oxygen Saturation (SpO2)** is a measure of the amount of haemoglobin that is bound to molecular oxygen at a given time point. The normal SpO2 level is around 95–100% (Radhakrishnan *et al*., **2019**).

**Electrodermal activity (EDA)** depends on the activation of eccrine sweat glands which are only stimulated by the SNS, having two parameters **s**kin conductance and skin resistance (Guinot Jimeno *et al*., **2011**). When the SNS is highly aroused, sweat gland activity increases, which in turn increases skin conductance (Roos *et al*., **2021**). Increases in skin conductance have a positive correlation with anxiety (Roos *et al.*, **2021**).

### 2.3.3. Biochemical parameters

Anxiety may be objectively evaluated by measuring the activation of the autonomic sympathetic nervous system, which is associated with the hypothalamic-pituitary-adrenal axis dysregulation. This axis acts through the hormone cortisol, which is produced in the adrenal cortex and affects many tissues. For analysis, cortisol can be sampled from the blood, the urine, and the saliva. It is expected a positive correlation between cortisol levels and anxiety (Roos *et al.*, **2021**).

The activation of the autonomic sympathetic nervous system also reduces pH. Therefore, it affects the saliva pH, as it leads to increased acidity and a decrease in oral pH (Roos *et al*., **2021**). Thus, a negative correlation between saliva pH and anxiety is expected (Roos *et al.*, **2021**). This correlation is also expected between urine pH and anxiety, and skin pH and anxiety. Skin pH appears to be a more useful psychophysical measure of anxiety, as it seems more controllable than salivary and urine pH, given that the latter can change if the subject takes substances orally (Sandin & Chorot, **1985**).

### 2.3.4. Behavioural parameters

Behavioural measures are not widely used due to the infrequent nature of many behaviours, the lack of experimental control, the potentially biasing effects of the presence of an observer, and ethical reasons (Major *et al*., **2000**). While these behaviours (e.g., trembling motor tension, speech dysfluencies) are not natural, for these to be observed in the laboratory, they were induced based on scenarios created with the information given by the participants about what makes them feel anxious.

### 2.3.5. Accelerometers

An accelerometer sensor, Figure 4, measures the acceleration of a moving object and can detect the frequency and intensity of human movement (Victorino *et al*., **2018**). Even if it is possible to find accelerometers with only one or two axes, the most common models have three (De Marsico & Mecca, **2017**). These sensors can be placed in different body parts such as the head, upper arm, forearm, thigh, waist, shin, and wrist. The more commonplace is on the wrist.

There are several types of these accelerometer sensors but the general principle is always the same, a mass is taken hung up by some force, such as a spring, and when an external force moves the sensor and consequently the mass, the device measures the movement (De Marsico & Mecca, **2017**). The position variation is converted into an electric signal-bearing in mind the direct proportionality among movement and acceleration (De Marsico & Mecca, **2017**).


Figure 4- AX3, Axivity accelerometer sensor, and wrist band. Source: Axivity, (**n.d.**).

Accelerometer sensors can be piezoelectric, internal electronic piezoelectric (IEPE), charge piezoelectric accelerometer, servo accelerometer, and capacitive accelerometer.

**Piezoelectric accelerometers** are self-generating devices characterized by an extended region of flat frequency response range, a large linear amplitude range, and excellent durability (Aszkler *et al.*, **2005**). It has these properties due to the use of piezoelectric material (e.g., quartz and polycrystalline ceramics) as the sensing element for the sensor. These sensors operate from frequencies as low as 2 Hz and up to about 5 kHz, they possess good off-axis noise rejection, high linearity, and a wide operating temperature range up to 120ºC (Fraden, **2016**). Piezoelectric accelerometers can be divided into two categories considering the mode of operation: IEPE and charge mode accelerometers.

**IEPE sensors** incorporate built-in, signal-conditioning electronics that function to convert the high-impedance charge signal generated by the piezoelectric sensing element into a usable low-impedance voltage signal that can be readily transmitted, over ordinary two-wire or coaxial cables, to any voltage readout or recording device (Aszkler *et al.*, **2005**). The simplicity of use, high accuracy, broad frequency range, and low cost of IEPE accelerometer systems make them the recommended type for use in most vibration or shock applications. The electronics within IEPE accelerometers require excitation power from a constant current, DC voltage source.

**Charge mode sensors** output a high-impedance, electrical charge signal that is generated directly by the piezoelectric sensing element (Aszkler *et al.*, **2005**). It should be mentioned that this signal is sensitive to corruption from environmental influences and cable-generated noise. Usually, charge mode accelerometers are used when high-temperature survivability is required.

**Capacitive accelerometers** are similar in operation to piezoresistive accelerometers, in that they measure a change across a bridge. Though instead of measuring a change in resistance, they measure a change in capacitance. A capacitive transducer is one of the proven and reliable elements that lends itself to micro miniaturization, high accuracy, and low cost (Aszkler *et al.*, **2005**).

**Servo accelerometers** keep the internal deflection of the proof mass to an extreme minimum. Electromagnetic forces, proportional to a feedback current, maintain the mass in a null position. As the mass attempts to move, a capacitive sensor typically detects its motion (Aszkler *et al.*, **2005**). A servo circuit derives an error signal from this capacitive sensor and sends a current through a coil, generating a torque proportional to acceleration, keeping the mass in capture or null mode. Servo accelerometers can cost up to ten times what other accelerometers cost.

### 2.3.6. Wrist accelerometer and physical activity

For decades, accelerometers have been widely used in monitoring functional motor movement, including studies on neuromuscular disorders like stroke and Parkinson's disease, and have focused on measuring gait. Body-worn accelerometers have also been utilized to classify activities in sitting, walking, standing, cycling, and lying positions, and have shown high accuracy in such studies (Victorino *et al.*, **2018**). A wrist accelerometer is the most widely used method in assessments of physical activity in population studies (Doherty, Jackson, Hammerla, Plo, et al., 2017). Given that they are small and low-cost, and have been designed and integrated into fashioned watches, bracelets, and bands, they can appeal to end-users for continuous and long-term use (Victorino *et al*., **2018**).

Several studies have been conducted to assess whether the physical capacity of the patient is affected by depression or anxiety disorders. In these studies, it is concluded that patients with these diseases have lower levels of physical capacity (Chung *et al.*, **2020**), but most of these articles evaluate this correlation by self-completion questionnaires.

The wrist accelerometer has shown good results in terms of validity for measuring physical activity in patients with schizophrenia and depression (Brien *et al*., **2017**; Schuch *et al.*, **2018**) and has already been used in studies assessing physical activity in patients with anxiety disorders (Dillon *et al.*, **2018**; Helgadóttir *et al.*, **2015**).

To conduct studies that evaluate physical activity using the accelerometer, a temporal quantity of data is necessary. Therefore, the literature has discussed what is the best length of days to record in order to have reliable data. A strong conclusion could not be reached as different populations have different characteristics (an older person does not have the same physical activity as a teenager). However, a significant number of studies use a duration of 7 days even though a conservative estimate of 3 to 7 days of valid data is acceptable (Broderick *et al.*, **2014**).

Accelerometers collect a lot of data such as **daily jerk (DJ)** a mean of the first derivative of acceleration magnitude, estimated using a five-sample linear regression (Brien *et al*., **2017**) that tells us if a subject is very active. This device can measure how much on average the device was accelerated within 1 min during the night and day (Brien *et al*., **2017**) resulting in the measures of **nocturnal physical activity (NPA)** and **daily physical activity (DPA).**

As one of the main functions of the accelerometer is to measure physical activity it is important to analyse the rhythm of the data recorded. For this, we have the measurements **interdaily stability (IS)** which indicates invariability of the 24 hours rhythm between days (Jones *et al*., **2005**), **intraday variability (IV)** which indicates fragmentation of rhythm (Jones *et al*., **2005**), and **relative amplitude (RA)** that indicates quantity of activity (Jones *et al*., **2005**).

Other measurements that the accelerometer allows to evaluate are the different **types of physical activity** (sedentary, light, moderate, and vigorous). When the metabolic equivalent intensity level is lower than 1.5 it is defined as a sedentary activity, light when it is between 1.5–3.99, moderate when it is between 4.00–6.99, or vigorous when it is higher than 7 (Esliger *et al.*, **2011**). The data from the accelerometer allows to measure the **duration of nocturnal immobility (NTID)**, **periods of night mobility (NTMP)**, **night mobility duration (NTMD)**, **periods of daytime immobility (DIP),** and **daytime immobility duration (DID)** with the Estimation of Stationary Sleep-segments method to measure This method uses the presence of long periods of idleness along with their duration in seconds as weights. Given that when the subject changes its sleeping posture we typically see interchanged now and then with short transitions with long periods of idleness (Borazio *et al*., **2014**).

# 3. Methodologies

This exploratory, quasi-experimental study was developed in the NM service of Hospital Particular de Almada, between April 2021 and January 2022, with two primary outcomes a) difference in STAI score between pre-exam and post-exam, and b) difference in physiological measures between pre-exam and post-exam. A convenience sample was divided into two groups, **Control group (CG)** and **Experimental group (EG)**, with the following inclusion criteria a) undergo a BS, b) have breast cancer, c) over 40 years old, d) be a woman, e) be able to write, speak and understand the Portuguese, and f) be able to communicate. All the patients included had clinical indications for BS and signed an informed consent form, allowing the use of their data for research purposes. To ensure patient confidentiality, their identification was coded. Both groups followed the normal protocol of *NuclearMed* and used a wrist accelerometer for three days before the exam (example: if the exam was on a Friday, patients were to use the wrist accelerometer on Tuesday, Wednesday, Thursday, and Friday until the end of the exam), with EG listen to music during imaging acquisition.

Our sample consisted of 30 participants who underwent BS with $^{99m}$Tc-HMDP, with a mean age of 57.70 years, divide into two groups in equal matter. Much of the sample were married (19 patients), employed (19 patients), and had secondary education (17 patients).

## 3.1. Selection of patients

Patient selection was carried out in two phases. A pre-recruitment phase in which patients were selected by the secretariat of the Hospital Particular de Almada when scheduling the BS study with 99mTc-HMDP and a second phase where patients were contacted by telephone.

In the first approach, the secretarial staff checked the inclusion criteria and, if these were met, a brief verbal explanation about the study was given. If they agreed to participate, they were given **Appendix A** (brief text explaining the study and asking for mobile phone contact, address, and e-mail).

In the second phase patients who agreed to participate in the pre-recruitment phase were contacted by telephone by the principal investigator, where an explanation of the study was once again given, and patients gave their verbal consent to participate. In this phase, they were told that if they had any doubts, they could clarify them by telephone at any time. They also were informed that the informed consent (see **Appendix B**), pre-exam questionnaire (see **Appendix C**), pre-exam STAI questionnaire (see **Appendix D**), and the wrist accelerometer would be sent to the address they had previously provided. These documents were sent to the participants' homes in order not to delay the NM service on the day of the exam and to allow them to familiarise themselves with the documents.

When patients agreed to participate in the study, they were assigned a number in ascending order of study participation. Patients who underwent BS for the first time were the first to be distributed in both groups sequentially, being numbered in order of invitation to participate in the study, with odd numbers in CG, and even numbers in EG, to obtain an equal number of participants in both groups with this particularity. The remaining patients scheduled for that day who accepted to participate were assigned to the two study groups sequentially, being numbered by order of invitation to participate in the study, with odd numbers in CG and even numbers in EG.

## 3.2. Selection of music

In this study, the music listened to by the participants was pre-selected. The music was chosen with the following criteria: a) between 60-80 beats per minute and b) instrumental music. As in a systematic review by de Witte *et al*. (**2020**), instrumental music and music with a slower tempo show better results in reducing anxiety than music with lyrics.

Considering these criteria, the song *Weightless* by Marconi Union was selected. This song has 71 beats per minute and is an instrumental song. The music was played from an MP4 and heard through headphones.

## 3.3. Ethical and Legal Procedures

The study was authorized by the Ethics Committee of the Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa (CE-ESTeSL-Nº.96 -2020 – **Appendix G**).

The patients that accepted being a part of this study had to sign their informed consent (**Appendix B**), which contain all necessary information about this research, such as the rights of the patient and the confidentiality of responses, anonymity of information, and the possibility of abandoning the study at any time during its execution.

For this study, we collected a variety of data including gender, age, education level, employability, the practice of physical activity, if the patient suffers from depression or anxiety disorders, if the patient was hypertensive or was taking antihypertensive medication, if the patient takes any anxiolytics/tranquilizers before the exam, what was the reason for the BS, if it was the first time having an NM examination, blood pressure, heart rate per minute, RR, SpO2, address, e-mail address, telephone contact. All these data were pseudo-anonymized, with only the investigator in charge of the NM Service being able to associate the cardinal numbers to the patient file.

Regarding the study material, specifically the results of the questionnaires, data records of the physiological measurements and the accelerometer data, were all digitalised and stored on a PC at ESTeSL. After the computerization of the answers to the questionnaires, the latter was destroyed.

## 3.4. Data collection instruments

In this study, we used several instruments some are in paper form and others are technologies. In the list below we list the instruments used:

**Blood pressure monitor:** The device measures blood pressure. Data was collected using OMRON M4-I (HEM-752A-E), OMRON MATSUSAKA Co., Ltd. Japan.

**Pulse oximeter:** The device measures the blood oxygen level. Data was collected using G-tech OLED GRAPH, Beijing Choice ElectronicTechnology Co., Ltd. China.

**Wrist accelerometer:** The device measures the vibration, or acceleration of motion and can detect the frequency and intensity of human movement (Victorino *et al.*, **2018**). Data was collected using Ax6, Axivity Ltd, United Kingdom.

**Portuguese short-form version of STAI**: The short-form State-Trait Anxiety Inventory is based on a 4-point Likert scale and consists of 8 questions (results range from 8 to 32). This questionnaire measures two types of anxiety, state anxiety and trait anxiety on a self-report basis here higher scores are correlated with higher levels of anxiety (Spielberger, Gorsuch & Lushene, **1983**; versão Portuguesa Silva, **2003**). See **Appendix D** and **Appendix E**.

**Pre-exam questionnaire**: This questionnaire gathers information about sociodemographic, health, and physical activity. This questionnaire is based on self-report and consists of 10 questions that are multiple-choice and/or open-ended. See **Appendix C.**

**Post-exam questionnaire:** This questionnaire is self-report based and consists of 4 multiple-choice questions. This questionnaire asks the patient questions related to the BS such as if they understand the information given about the exam, if they felt anxious, and if yes in which phase (before, during, or after the BS). If they listen to music, they will have to answer questions such as, if the music help reduces the level of anxiety and if they felt that the music was the right one to reduce anxiety. See **Appendix F.**

## 3.5. Before, During, and After Bone Scintigraphy

Before the exam patients were contacted 4 days prior to remind them to place the wrist accelerometer on the non-dominant side (if this was not possible, the patient had to place the wrist accelerometer on the dominant side). They were also told to wear it all the time until the end of the procedure (the accelerometer is waterproof), but if they felt discomfort or if it was necessary, they could take it off.

On the day of the exam, Figure 5, when the patient arrives at the NM department and confirms her presence, patients of both groups deliver the informed consent (**Appendix B**) and the pre-exam questionnaires in paper form filled out (**Appendix C**) and the pre-exam STAI (**Appendix D**) to be completed after the physiological measurements (BP, HR, RR, and SpO2) were gathered. If the patients had any doubt about the informed consent or the pre-exam questionnaire they were answered before any other procedure was carried out. Before the injection of the radiopharmaceutical, physiological measurements (BP, HR, RR, and SpO2) were collected using a pulse oximeter and a blood pressure monitor, the STAI questionnaire was also administered. The values obtained were recorded on a paper register with a cardinal number assigned at the time of acceptance of participation in the study. Moreover, patients wore a wrist accelerometer for 3 days before the exam.

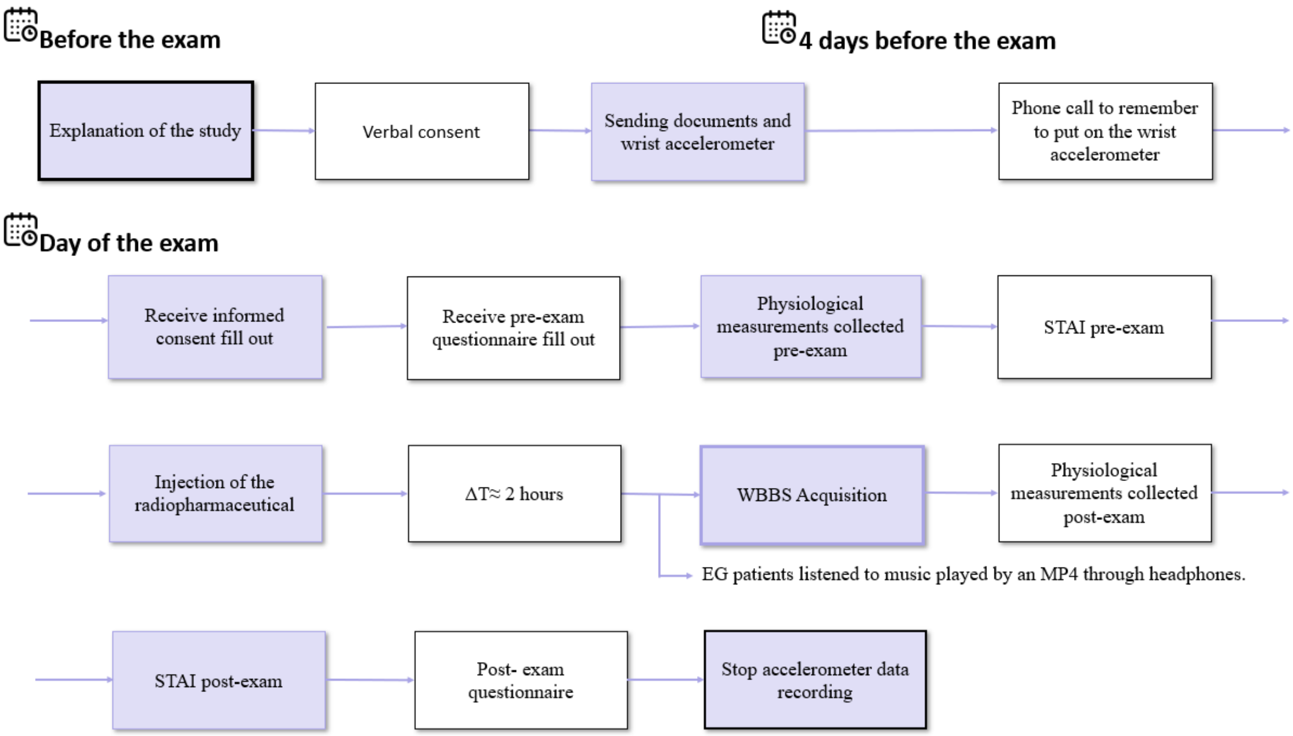


Figure 5- Procedure flowchart.

During image acquisition, the CG followed the standard BS protocol (**Appendix H**), whilst the EG followed the same protocol with the addition of listening to pre-selected music during imaging acquisition.

After the imaging acquisition of BS physiological measurements (BP, HR, RR, and SpO2) were taken again, and the patients fill in the STAI questionnaire (**Appendix E**), and a post-exam questionnaire regarding the experience of the procedure carried out (**Appendix F**). The wrist accelerometer was stopped recording movements after these procedures were completed, and afterward, the data was extracted.

## 3.6. Statistical analysis

The data were analysed in the statistical software SPSS®, version 26.0 for Windows®. For the normality, the Shapiro-Wilk test was applied. The results were considered significant at a 5% significance level. The statistical analysis carried out was as follows:

- To characterise the collected sample, frequency analysis (n, %) was used for qualitative data, and for quantitative data, we used the calculation of minimum, maximum, mean, and standard deviation.
- To compare the two moments of assessment (pre-and post-exam) in each group the t-test for paired samples (when the assumption of normality was verified) and the paired Wilcoxon test (when it was not verified) were used.
- To study the relationship between two variables, the Pearson correlation coefficient (when the normality assumption was verified) or Spearman correlation coefficient (when it was not verified), or Eta correlation (between a categorical and a scale variable) was used.
- For the comparison of the two independent groups, the t-test (when the normality assumption was verified) or the Mann-Whitney test (when the normality of the sample was not verified) was used. Categorical variables were analysed by Fisher’s exact test.

# 4. Results

In the present study, a sample of 30 female patients who underwent clinically indicated BS at *NuclearMed* was included. This sample was divided into two groups, 15 in each group. Most patients had performed this study before, but only 5 patients in CG and 5 in EG performed this study for the first time.

When assessing the descriptive and sociodemographic measures of the sample, Table 1, it was found that the participants' **age** ranged between 45 and 73 years, with a mean value of 57.70±8.09 years. The CG age varied between 45 and 73 years, with a mean value of 57.27±9.48 years. In the EG age ranged between 45 and 72 years, with a mean score of 58.13±6.73 years.

Regarding **academic qualifications** in the sample 9 (30.0%) had primary education, 17 (56.7%) had secondary education, 3 (10.0%) had a bachelor's degree and 1 (3.3%) had a master's degree. Concerning **civil status** and **employment**, the majority were married 19 (63.3%) and 19 (63.3%) had a job. Through the clinical records, Table 1, we learned that in the CG 26.7% of patients were in the follow-up phase, 20.0% chemotherapy, 20.0% hormonal, 13.3% in the initial staging, and 6.7% radiotherapy. In EG 53.3% were in the initial staging, 20.0% hormonal, and 13.3% chemotherapy. In the sample, we do not know at what stage of treatment 4 patients were.

No statistically significant association between age, stages of treatment, academic degree, civil status, employment, and the group was found ($p>0.05$), Table 1. Concerning academic degree and civil status, the sample for both groups are identical ($p= 1.000$).

Table 1- Socio-demographic and clinical characterisation of breast cancer patients included in the sample .

| | CG | | | | EG | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **n (%)** | **Min** | **Max** | **Mean ± SD** | **n (%)** | **Min** | **Max** | **Mean ± SD** | **p** |
| **Sex** | | | | | | | | | |
| Female | 15 (100.0) | | | | 15 (100.0) | | | | |
| Male | 0 (0.0) | | | | 0 (0.0) | | | | |
| **Age (years)** | | 45 | 73 | 57.27±9.48 | | 45 | 72 | 58.13±6.73 | 0.775* |
| **Stages of treatment** | | | | | | | | | 0.359† |
| Initial staging | 2 (13.3) | | | | 8 (53.3) | | | | |
| Follow-up | 4 (26.7) | | | | 0 (0.0) | | | | |
| Chemotherapy | 3 (20.0) | | | | 2 (13.3) | | | | |
| Radiotherapy | 1 (6.7) | | | | 0 (0.0) | | | | |
| Hormonal | 3 (20.0) | | | | 3 (20.0) | | | | |
| **Academic degree** | | | | | | | | | 1.000† |
| Primary education | 4 (26.7) | | | | 5 (33.3) | | | | |
| Secondary education | 8 (53.3) | | | | 9 (53.3) | | | | |
| Bachelor’s degree | 2 (13.3) | | | | 1 (13.3) | | | | |
| Master’s degree | 1 (6.7) | | | | 0 (6.7) | | | | |
| PhD | 0 (0.0) | | | | 0 (0.0) | | | | |
| **Civil Status** | | | | | | | | | 1.000† |
| Married | 10 (66.7) | | | | 9 (60.0) | | | | |
| Divorced | 2 (13.3) | | | | 3 (20.0) | | | | |
| Single | 2 (13.3) | | | | 1 (6.7) | | | | |
| Widow | 1 (6.7) | | | | 1 (6.7) | | | | |
| **Employment** | | | | | | | | | 0.716* |
| Employed | 9 (60.0) | | | | 10 (66.7) | | | | |
| Not employed | 6 (40.0) | | | | 5 (33.3) | | | | |

Min- Minimum; Max- Maximum; SD- standard deviation; CG- control group; EG- experimental group. * Independent t-test; † Fisher Exact Test.

## 4.1. Results of the Pre-exam Questionnaire

The pre-exam questionnaire (**Appendix C**) collected information such as practised physical activity, medical information, the reason for the examination, and previous examination in nuclear medicine, to name a few. The answers to the pre-exam can be found in **Appendix H.**

### 4.1.1. Practised physical activity

The patients in the pre-exam questionnaire were asked whether they had practiced any kind of physical activity in the 3 days prior to the exam, 6 participants said yes (20.0%), Table 2. Of those who practiced physical activity, these were aerobics, Zumba, walking, gym machines, and physiotherapy (arm exercises). Using an independent t-test we found that the sample for both groups is identical (p= 1.000).

Table 2- Frequency analysis to the question "Did you engage in physical activity in the 3 days before undergoing bone scintigraphy?".

| | **CG** | **EG** | |
|---|---|---|---|
| | **n (%)** | **n (%)** | **p** |
| **Practiced physical activity** | | | |
| Yes | 3 (20.0) | 3 (20.0) | 1.000* |
| No | 12 (80.0) | 12 (80.0) | |

CG- control group; EG- experimental group; * Independent t-test.

### 4.1.2. Medical information

Respecting the medical information, Table 3, 70.0% of participants did not suffer from depression and/or anxiety. In CG 1 person suffers from anxiety, 1 from depression, and 1 from anxiety and panic attacks. In EG 3 people suffer from anxiety, 2 from depression, and 1 from depression, anxiety, and panic attacks. As such in EG more people suffer from depression and anxiety than in the CG.

Concerning medications taken by the participants, 8 participants (26.7%) said they took anxiolytics before the exam. It should be noted that in the EG almost half of the patients take this medication, which is consistent with the number of participants in this group suffering from depression or anxiety disorders. In relation to having hypertension or taking antihypertensive medication, 20 participants affirmed negatively (66.7%). It is to be noted that EG has a more heterogeneous group in this variant than CG. No statistically significant association between depression and/or anxiety disorder, hypertension, and the group was found (p>0.05). Since anxiolytic before the exam p <0.05, we have sufficient evidence to say that there is a significant association between anxiolytic before the exam and group.

Table 3- Frequency analysis of pre-exam questionnaire questions: "Do you suffer from depression or anxiety disorder?"," Are you hypertensive or on antihypertensive therapy?" and "Did you take any anxiolytic before the exam?".

| | CG<br>n (%) | EG<br>n (%) | p |
|---|---|---|---|
| **Depression and/or anxiety disorder** | | | |
| Yes | 3 (20.0) | 6 (40.0) | 0.247* |
| No | 12 (80.0) | 9 (60.0) | |
| **Anxiolytic before the exam** | | | |
| Yes | 1 (6.7) | 7 (46.7) | 0.014* |
| No | 14 (93.3) | 8 (53.3) | |
| **Hypertension or Antihypertensive therapy** | | | |
| Yes | 4 (26.7) | 6 (40.0) | 0.456* |
| No | 11 (73.3) | 9 (60.0) | |

CG- control group; EG- experimental group; * Independent t-test.

### 4.1.3. Perception of why the exam was carried out

In the study sample, 96.7% of patients reported knowing the clinical reason why they came for a BS. The main clinical indication was staging after BC diagnosis (CG- 46.7%; n= 7 and EG- 28.6%; n= 4), Figure 6. Other clinical indications were investigation of secondary lesions, generalised pain, and evaluation of hormone therapy response. Of all clinical indications, pain was the most relevant in the sample with 27.6%, n= 8.

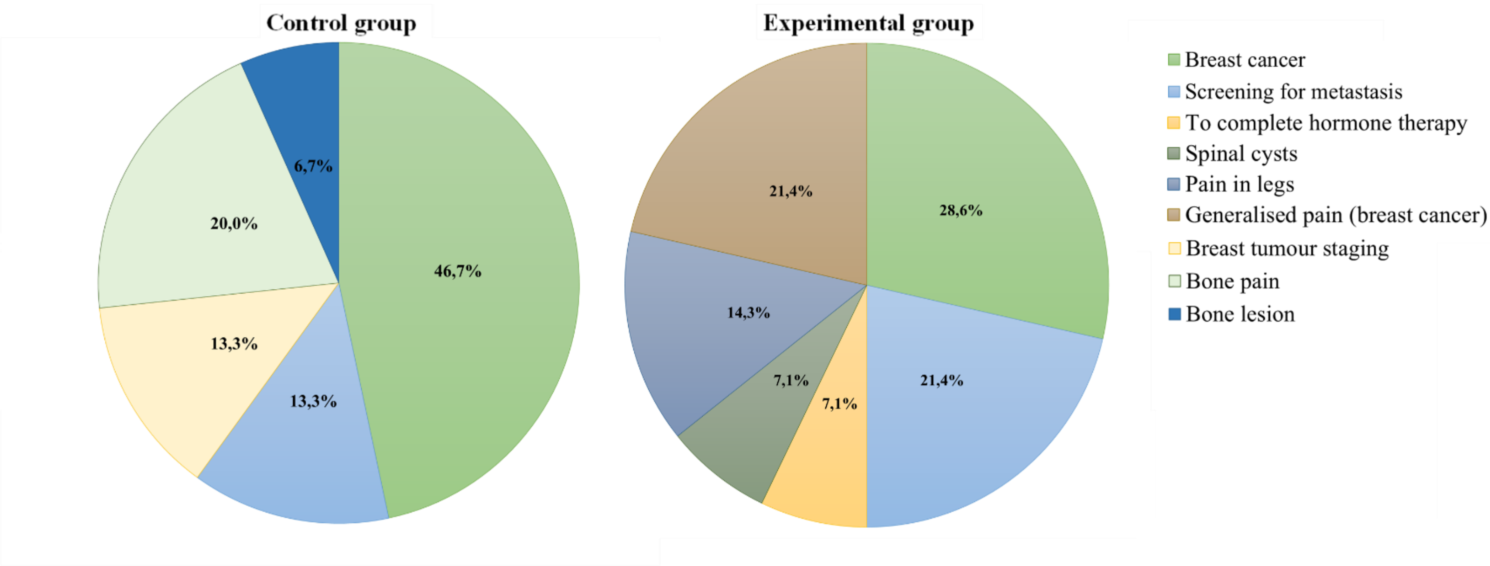


Figure 6- Pie-chart graphs of the answers to “What is the reason for undergoing bone scintigraphy?”.

### 4.1.4. Previous examination in nuclear medicine

One of the questions in the pre-exam questionnaire consisted of knowing whether the patients had already had NM exams, and 80% of the patients answered affirmatively, Table 4. Of those who had an NM exam, the majority previously had undergone a BS (CG- 66.7%, n= 10; EG- 66.7%, n= 10), Figure 7. It should be noted that the participants also said MRI and bone densitometry even though these are radiology exams.

Table 4 - Frequency analysis of the question “Is this the first time you are undergoing a nuclear medicine exam?”.

| | CG n (%) | EG n (%) | p |
|---|---|---|---|
| **First Time performing NM exam** | | | |
| Yes | 2 (13.3) | 4 (26.7) | 0.379* |
| No | 13 (86.7) | 11 (73.3) | |

CG- control group; EG- experimental group; * Independent t-test.

In our sample, we have 10 patients who have never undergone a BS, being divided equally by CG and EG. Of these 10 patients, 6 never had an NM examination (2 in CG and 4 in EG), Figure 7, and 4 had other NM examinations ( 3 in CG and 1 in EG).

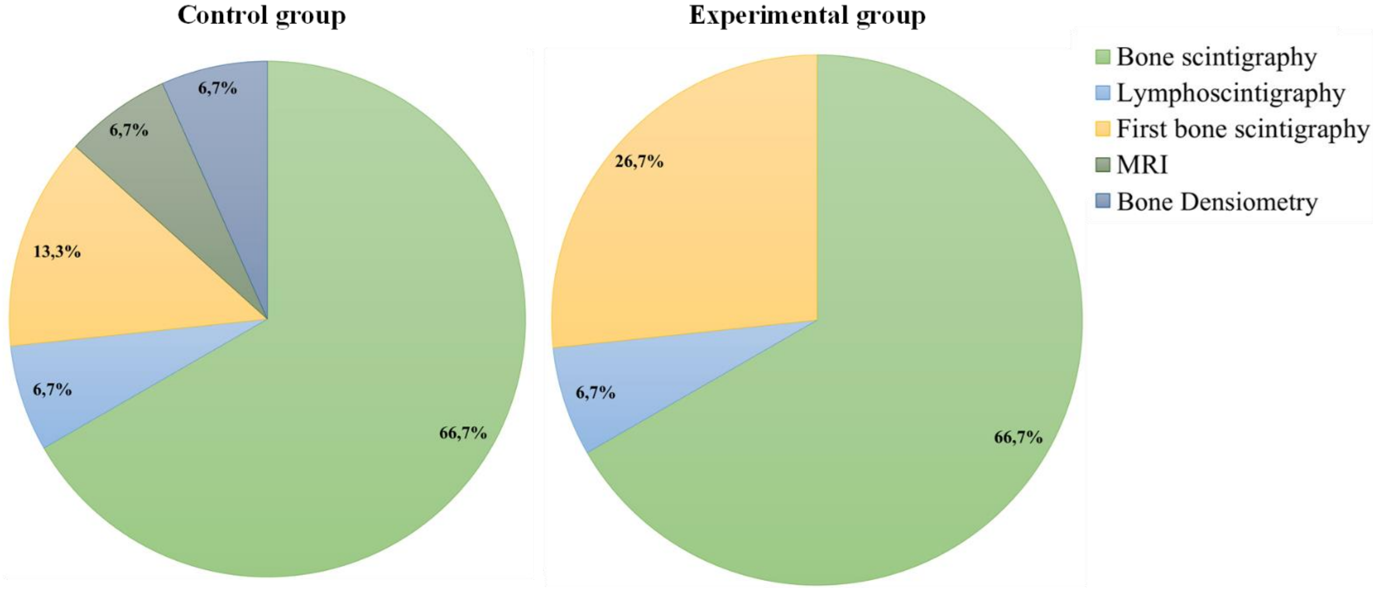


Figure 7- Pie-chart graphs of the answers to “What nuclear medicine exams you previously had?”. If this is the first bone scintigraphy the patient undergoes the results are shown as First bone scintigraphy.

## 4.2. Results of Physiological measurements

The physiological measurements were collected before the injection of the radiopharmaceuticals and after imaging acquisition (results present in **Appendix I** and **Appendix J**), using a blood pressure monitor for BP and HR, a pulse oximeter for SpO2, and counting the number of breaths for an entire minute for RR.

Upon observing the mean values of the physiological measures, Table 5, we found that pre- and post-exam systolic **BP** (CG pre-exam: 134.07±20.37; CG post-exam: 137.33±18.14; EG pre-exam: 133.67±16.37; EG post-exam: 133.33±13.34) in both groups is considered elevated (mean values higher than 120 mmHg). Although the mean diastolic BP value, Table 5, for the EG is less than 80 mmHg pre- and post-exam, we consider that the diastolic BP is also elevated due to the large standard deviation obtained in this group (pre-exam: 78.67±11.44; post-exam: 79.93±12.36), we also consider that the diastolic BP for the CG is high (pre-exam: 83.07±11.85; post-exam: 81.67±9.90). It can be seen that the mean pre-exam systolic BP values are slightly bigger in the CG than in the EG, the same occurring in the post-exam. In addition, we verify an increase in systolic BP in CG and a very small decrease in EG after BS.

Now, in the pre- and post-exam the CG values for diastolic BP are higher than the EG values, with a decrease in CG values and an increase in EG after the exam. Comparing the pre-exam BP levels between the CG and EG, it was verified that there were no significant differences (Systolic BP pre-exam: U= 106.000, p= 0.787; Diastolic BP pre-exam: t= 1.035, p= 0.310; Systolic BP post-exam: U= 100.000, p= 0.603; Diastolic BP post-exam: t= 0.424, p= 0.675) nor with regard to the differences between pre-and post-exam (Systolic BP pre-post-exam CG: t= -0.797, p= 0.439; Diastolic BP pre - post-exam CG: t=0.632, p= 0.538; Systolic BP pre - post-exam EG: Z= -0.483, p= 0.629; Diastolic BP pre - post-exam EG: t= -0.492, p=0.630), Table 6.

Normal mean values are seen for **HR** (60-100 beats per minute) in both groups (CG pre-exam: 79.27±14.41; CG post-exam: 78.40±9.50; EG pre-exam: 83.93±13.80; EG post-exam: 86.87±13.12), Table 5. As we can see EG values are higher than in CG in the pre- and post-exam. Also, we observe a slight decrease in CG and an increase in EG after BS. Evaluating HR, between the CG and the EG it was found that there were no significant differences in the pre-exam (HR pre-exam: t= -0.906, p= 0.373) nor regarding the differences between the groups before the exam, Table 6. Furthermore, statistically significant differences were detected regarding post-exam HR (post-exam HR: t= -2.024, p= 0.053).

Table 5- Statistical analysis of physiological measurements before and after bone scintigraphy in the control and experimental group.

| | **Physiological measurements before BS** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **CG (n=15)** | | | **EG (n=15)** | | | |
| | **Min** | **Max** | **Mean ± SD** | **Min** | **Max** | **Mean ± SD** | **p** |
| Systolic BP (mmHg) | 104 | 183 | 134.07±20.37 | 100 | 158 | 133.67±16.37 | 0.787** |
| Diastolic BP (mmHg) | 68 | 102 | 83.07±11.85 | 58 | 103 | 78.67±11.44 | 0.310* |
| HR (beats/minute) | 64 | 112 | 79.27±14.41 | 61 | 110 | 83.93±13.80 | 0.373* |
| RR (breaths/minute) | 12 | 19 | 14.60±2.20 | 10 | 20 | 14.60±2.82 | 0.867** |
| SpO2 (%) | 93 | 99 | 96.73±2.22 | 95 | 99 | 97.33±1.50 | 0.611** |
| | **Physiological measurements after BS** | | | | | | |
| | **CG (n=15)** | | | **EG (n=15)** | | | |
| | **Min** | **Max** | **Mean ± SD** | **Min** | **Max** | **Mean ± SD** | **p** |
| Systolic BP (mmHg) | 114 | 177 | 137.33 ± 18.14 | 104 | 161 | 133.33 ± 13.34 | 0.603** |
| Diastolic BP (mmHg) | 60 | 96 | 81.67 ± 9.90 | 61 | 113 | 79.93 ± 12.36 | 0.675* |
| HR (beats/minute) | 65 | 98 | 78.40 ± 9.50 | 67 | 111 | 86.87 ± 13.12 | 0.053* |
| RR (breaths/minute) | 9 | 20 | 15.53 ± 3.07 | 8 | 18 | 14.20 ± 2.93 | 0.234* |
| SpO2 (%) | 93 | 99 | 93.13 ± 1.85 | 94 | 99 | 97.47 ± 1.73 | 0.039** |

Min- Minimum; Max- Maximum; SD- standard deviation; BS- bone scintigraphy; CG- control group; EG- experimental group; Systolic BP- systolic blood pressure; Diastolic BP- diastolic blood pressure; HR- heart rate; RR- respiratory rate; SpO2- Blood Oxygen Saturation; * Independent t-test; **Mann-Whitney.

Likewise in **RR**, mean values are considered normal (12-20 breaths per minute) for both groups (CG pre-exam: 14.60±2.20; CG post-exam: 15.53±3.07; EG pre-exam: 14.60±2.82; EG post-exam: 14.20±2.93), Table 5. Comparing the values in each group before and after BS we see that CG has somewhat bigger values than EG. It is to be highlighted that in the EG the pre-post-exam values are very similar. Additionally, a small increase in CG and a small decrease in EG post-exam are noted. Between CG and EG no significant differences in the pre-and post-exam were found (RR pre-exam: U= 108.500, p= 0.867; RR post-exam: t= 1.217, p=0.234) nor regarding the differences between pre- and post-exam, Table 6.

Table 6- Results of the paired t-test and Wilcoxon signed ranks test in the control and experimental group for various physiological differences.

| | | **Paired t-test** | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 95% Confidence Interval of the Difference | | | | |
| **Group** | **Paired Differences** | **Mean ±SD** | **Std. Error Mean** | **Lower** | **Upper** | **t** | **df** | **p** |
| CG | Systolic BP before–Systolic BP after | -3.267±15.868 | 4.097 | -12.054 | 5.521 | -0.797 | 14 | 0.439 |
| CG | Diastolic BP before–Diastolic BP after | 1.400±8.584 | 2.216 | -3.354 | 6.154 | 0.632 | 14 | 0.538 |
| CG | HR before–HR after | 0.867±13.394 | 3.458 | -6.551 | 8.284 | 0.251 | 14 | 0.806 |
| EG | Diastolic BP before–Diastolic BP after | -1.267±9.975 | 2.575 | -6.790 | 4.257 | -0.492 | 14 | 0.630 |
| EG | HR before–HR after | -2.933±11.955 | 3.087 | -9.554 | 3.687 | -0.950 | 14 | 0.358 |
| EG | RR before–RR after | 0.400±2.640 | 0.682 | -1.062 | 1.862 | 0.587 | 14 | 0.567 |

| | | **Wilcoxon Signed Ranks Test** | |
|---|---|---|---|
| **Group** | **Paired Differences** | **Z** | **p** |
| CG | RR before–RR after | -1.548 | 0.122 |
| CG | SpO2 before–SpO2 after | -0.976 | 0.329 |
| EG | Systolic BP before–Systolic BP after | -0.483 | 0.629 |
| EG | SpO2 before–SpO2 after | -0.159 | 0.873 |

SD- standard deviation; df- degrees of freedom; BS- bone scintigraphy; CG- control group; EG- experimental group; Systolic BP- systolic blood pressure; Diastolic BP- diastolic blood pressure; HR- heart rate; RR- respiratory rate; SpO2- Blood Oxygen Saturation.

The mean value of **SpO2**, Table 5, tells us that an abnormal level is identified in post-exam CG (93.13±1.85), given that the normal level is around 95–100%. In contrast that does not happen for pre-post exam EG and pre-exam CG (CG pre-exam: 96.73±2.22; EG pre-exam: 97.33±1.50; EG post-exam: 97.47±1.73). A similar result is obtained in pre-and post-exam in the EG, while in CG the value decreases after the exam. Evaluating SpO2, between the CG and the EG it was found that there were no significant differences in the pre-exam (SpO2 pre-exam: U= 100.500, p= 0.611) nor regarding the differences between pre-and post-exam, Table 6. On the other hand, between the two groups statistically, significant differences were detected regarding post-exam SpO2 (SpO2 post-exam: U= 64.000, p= 0.039).

## 4.3. Results of the STAI Questionnaires

The STAI questionnaires were completed by the participants before radiopharmaceutical injection and after imaging acquisition (results available in **Appendix K** and **Appendix L**). Afterward, the STAI score was obtained for each patient.

A mean value of the STAI scores pre- and post-scan was obtained for the CG and EG. It is noticeable that the STAI levels were slightly higher for the CG (pre-exam: 21.27±3.56; post-exam: 20.00±5.63) when compared to the EG pre-post exam (pre-exam: 19.73±4.38; post-exam: 19.27±5.01), and that the STAI scores decrease in both groups after the scan. Between the two groups, no statistically significant differences in STAI levels were detected in the pre-scan (U= 89.000, Z= -0.981, p> 0.05), nor in the post-scan (U= 111.000, Z= -0.063, p= 0.950), Table 7.

No statistically significant differences in pre-post scan STAI-S scores were found between patients undergoing the exam for the first time and patients who had undergone it before (pre-exam CG: U= 18.000, Z=-0.529, p= 0.597; post-exam CG: U= 17.000, Z=-0.658, p= 0.511; pre-exam EG: U= 15.000, Z= -1.232, p= 0.218; post-exam EG: U= 21.500, Z=-0.432, p= 0.666). Also, no statistically significant differences in pre-post scan STAI-S scores were found between patients that practise physical activity and does who did not (pre-exam CG: U= 16.500, Z=-0.219, p= 0.826; post-exam CG: U= 13.500, Z=-0.654, p= 0.513; pre-exam EG:  U= 9.000, Z= -1.307, p= 0.233; post-exam EG: U= 15.000, Z= -0.437, p= 0.662).

A Wilcoxon signed rank test revealed that STAI score in CG were not significantly lower after the intervention (*Mdn*= 21.00, n= 15) compared to before (*Mdn*= 21.00, n= 15), Z= -0.716, p= 0.474, with a small effect number r= 0.18, nor in EG (*Mdn* = 20.00, n= 15) compared to before (*Mdn*= 21.00, n= 15), Z= -0.176, p= 0.861, with a very small effect number *r*= 0.05. The same test was applied to the STAI results without being differentiated into groups, revealing that STAI scores were once again not significantly lower after the intervention (*Mdn*= 21.00, n= 30) compared to before (*Mdn*= 20.00, n= 30), Z= -0.366, p= 0.714, with a small effect number r=0.07.

Table 7 – STAI scores pre- and post-scan in both groups.

| | | Group statistics | | | Test statistics | | |
|---|---|---|---|---|---|---|---|
| | **Group (n=)** | **Min** | **Max** | **Mean ± SD** | **U** | **Z** | **p** |
| STAI pre-exam | CG (n=15) | 17 | 30 | 21.27 ± 3.56 | 89.000 | -0.981 | 0.327 |
| | EG (n=15) | 9 | 27 | 19.73 ± 4.38 | | | |
| STAI post-exam | CG (n=15) | 8 | 32 | 20.00 ± 5.63 | 111.000 | -0.063 | 0.950 |
| | EG (n=15) | 8 | 25 | 19.27 ± 5.01 | | | |

CG- control group; EG- experimental group; Min- Minimum; Max- Maximum; SD- standard deviation.

## 4.4. Results of the accelerometer data

The participants wore the wrist accelerometer for three days (for example: if the exam was on a Friday, they wore it Tuesday, Wednesday, Thursday, and Friday until the end of the procedure). After data collection, we extrapolate a variety of data from the accelerometer, obtaining a report as shown in Figure 8.

In the initial analysis of the data obtained by the accelerometers, we found that the WT on some days was less than 21 hours. As we need at least 21 hours of data to analyse the data, the days on which this does not happen were excluded. Thus, in the EG we have data from 14 participants and in the CG, we have data from 12 participants, since in two patients of this group on all days of data recording, we have a WT of less than 21 hours. Also, in CG we have two reports that only have WT> 21 hours on the third day, for these reports it was impossible to make a comparison with the other days. On the first day of recording, WT is smaller than 21 hours in all patients.

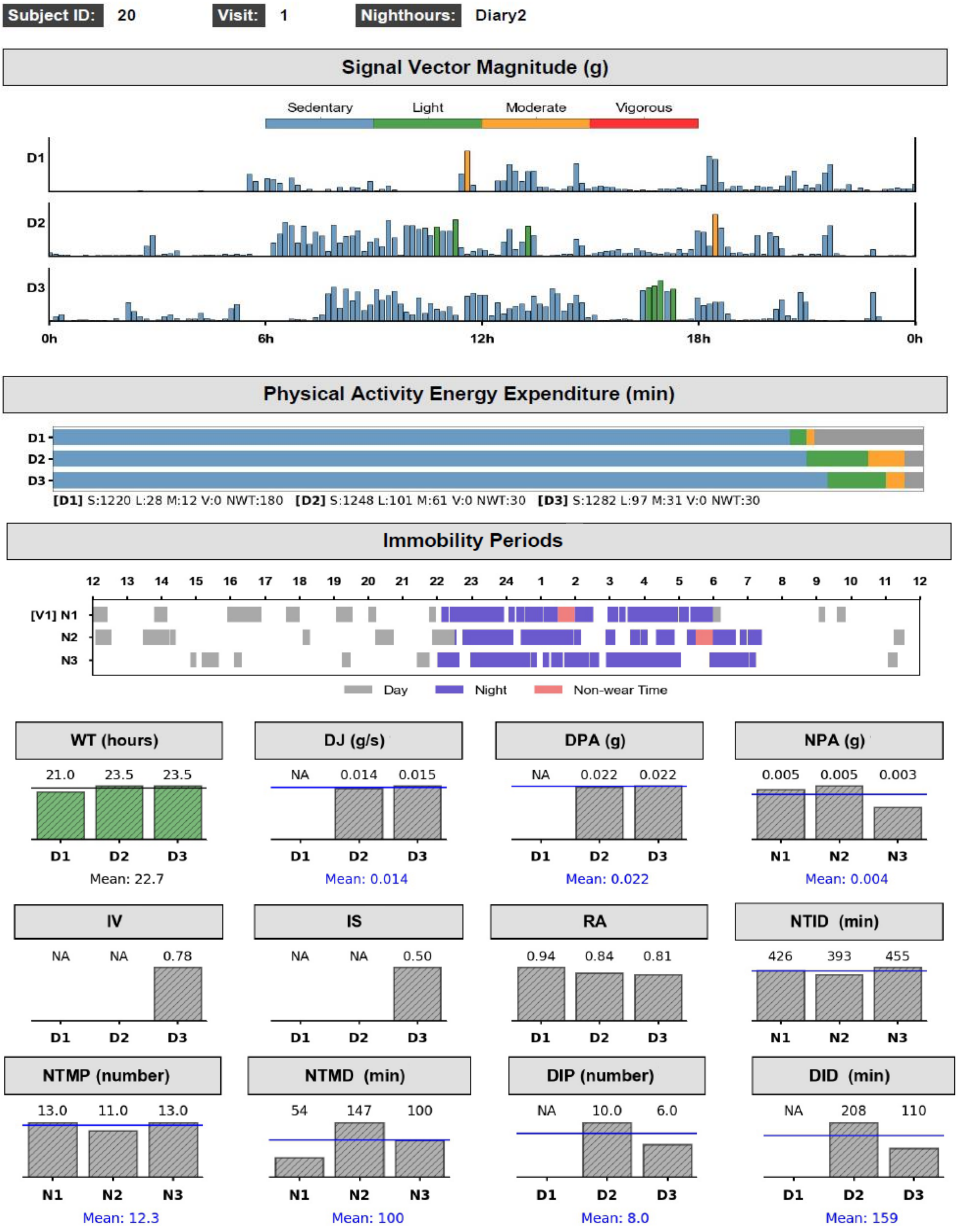


Figure 8- Report of the analysis of the data from the accelerometer of patient 20. Abbreviations: WT- wear time; DJ- daily jerk; NPA- nocturnal physical activity; DPA-daily physical activity; IS- interdaily stability; IV- intraday variability; RA- Relative amplitude; NTID- duration of nocturnal immobility; NTMP- periods of night mobility; NTMD- night mobility duration; DIP- periods of daytime immobility; DID- daytime immobility duration.

In Table 8, we can see that the mean WT is very close to 24 hours in both groups. Regarding DJ, NPA and DPA similar mean results were obtained between CG and EG (CG: DJ= 0.02±0.01; NPA= 0.01±0.00; DPA= 0.03±0.02. EG: DJ= 0.02±0.01; NPA= 0.00±0.00; DPA= 0.04±0.01). As for IS, RA, NTID and NTMP we observe that these values are bigger in EG (IS= 0.61±0.09; RA= 0.92±0.05; NTID= 406.66± 80.48; NTMP=26.21±75.72) than in CG (IS= 0.57±0.13; RA= 0.89±0.08; NTID= 383.45±97.29; NTMP= 9.80±4.25). On the contrary CG has bigger values than EG for IV, NTMD, DIP and DID (CG: IV= 0.94±0.18; NTMD= 107.18±79.35; DIP= 10.18±6.41; DID= 208.27±145.84; EG: IV= 0.77±0.21; NTMD= 82.86±48.27; DIP= 6.07±4.61; DID= 121.88±132.47).

Regarding the physical activity energy expenditure, Table 9, we observe that the participants spend more time in sedentary behaviour with an average of 1146.76±142.24 minutes, and less time in vigorous activity 2.08±9.48 minutes. The same occurred in CG (Sedentary: 1186.88±140.61; Vigorous: 3.04±12.95) and EG (Sedentary: 1113.33±134.75; Vigorous: 1.28±4.85). Between the two groups, the patients spend more time in light, and moderate activity in EG and sedentary and vigorous activity in CG.

Table 8- Statistical analysis of the different data obtained from the accelerometers.

| | **All (n= 26)** | | | **CG (n= 12)** | | | **EG (n= 14)** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Min** | **Max** | **Mean±SD** | **Min** | **Max** | **Mean±SD** | **Min** | **Max** | **Mean±SD** |
| **WT (hours)** | 20.50 | 24.00 | 23.51±0.71 | 20.50 | 24.00 | 23.40±0.85 | 22.00 | 24.00 | 23.60±0.55 |
| **DJ (g/s)** | 0.00 | 0.04 | 0.02±0.01 | 0.00 | 0.03 | 0.02±0.01 | 0.01 | 0.04 | 0.02±0.01 |
| **NPA (g)** | 0.00 | 0.02 | 0.00± 0.00 | 0.00 | 0.02 | 0.01±0.00 | 0.00 | 0.01 | 0.00±0.00 |
| **DPA (g)** | 0.00 | 0.08 | 0.03 ±0.02 | 0.01 | 0.08 | 0.03±0.02 | 0.00 | 0.06 | 0.04±0.01 |
| **IS** | 0.37 | 0.77 | 0.60±0.11 | 0.37 | 0.76 | 0.57±0.13 | 0.48 | 0.77 | 0.61±0.09 |
| **IV** | 0.44 | 1.22 | 0.85±0.22 | 0.59 | 1.22 | 0.94±0.18 | 0.44 | 1.22 | 0.77±0.21 |
| **RA** | 0.72 | 365.35 | 8.16±50.26 | 0.72 | 0.99 | 0.89±0.08 | 0.77 | 0.98 | 0.92±0.05 |
| **NTID (min)** | 8.00 | 592.85 | 389.14±103.85 | 97.33 | 577.90 | 383.45±97.29 | 279.47 | 592.85 | 406.66±80.48 |
| **NTMP (number)** | 0.00 | 425.95 | 20.75±57.90 | 0.00 | 18.00 | 9.80±4.25 | 0.00 | 425.95 | 26.21±75.72 |
| **NTMD (min)** | 10.87 | 345.53 | 93.30±65.86 | 10.87 | 345.53 | 107.18±79.35 | 15.67 | 241.42 | 82.86±48.27 |
| **DIP (number)** | 0.00 | 25.00 | 7.92±5.86 | 1.00 | 25.00 | 10.18±6.41 | 0.00 | 20.00 | 6.07±4.61 |
| **DID (min)** | 0.00 | 591.73 | 160.67±145.14 | 15.78 | 514.83 | 208.27±145.84 | 0.00 | 591.73 | 121.88±132.47 |

Min- Minimum; Max- Maximum; SD- standard deviation; CG- control group; EG- experimental group; WT- wear time; DJ- daily jerk; NPA- nocturnal physical activity; DPA-daily physical activity; IS- interdaily stability; IV- intraday variability; RA- Relative amplitude; NTID- duration of nocturnal immobility; NTMP- periods of night mobility; NTMD- night mobility duration; DIP- periods of daytime immobility; DID- daytime immobility duration.

We found that the day before the exam (day 3) patients have more drowsy periods during the day and stay in these periods for a longer duration compared with the other days (DIP: Day 2= 7.04±5.82; Day 3= 8.60±5.88; DID: Day 2= 139.75±133.70; Day 3= 179.01±155.19. Some patients have this characteristic more expressed than others as seen in ID 18, Figure 9. We see this state happen in 12 of 26 reports, 7 reports in CG, and 5 reports in EG

Table 9- Statistical analysis of the different types of physical activity.

| | Physical activity Energy Expenditure (minutes) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | All (n=26) | | | CG (n=12) | | | EG (n=14) | | |
| | **Min** | **Max** | **Mean ± SD** | **Min** | **Max** | **Mean ± SD** | **Min** | **Max** | **Mean ± SD** |
| Sedentary | 804.00 | 1409.00 | 1146.76±142.24 | 914.00 | 1409.00 | 1186.88±140.61 | 804.00 | 1324.00 | 1113.33±134.75 |
| Light | 11.00 | 232.00 | 128.95±57.77 | 11.00 | 207.00 | 105.80±52.20 | 43.00 | 232.00 | 148.23±55.04 |
| Moderate | 2.00 | 365.00 | 132.76±88.88 | 2.00 | 289.00 | 108.28±82.97 | 19.00 | 365.00 | 153.17±88.50 |
| Vigorous | 0.00 | 66.00 | 2.08±9.48 | 0.00 | 66.00 | 3.04±12.95 | 0.00 | 27.00 | 1.28±4.85 |

Min- Minimum; Max- Maximum; SD- standard deviation; CG- control group; EG- experimental group.

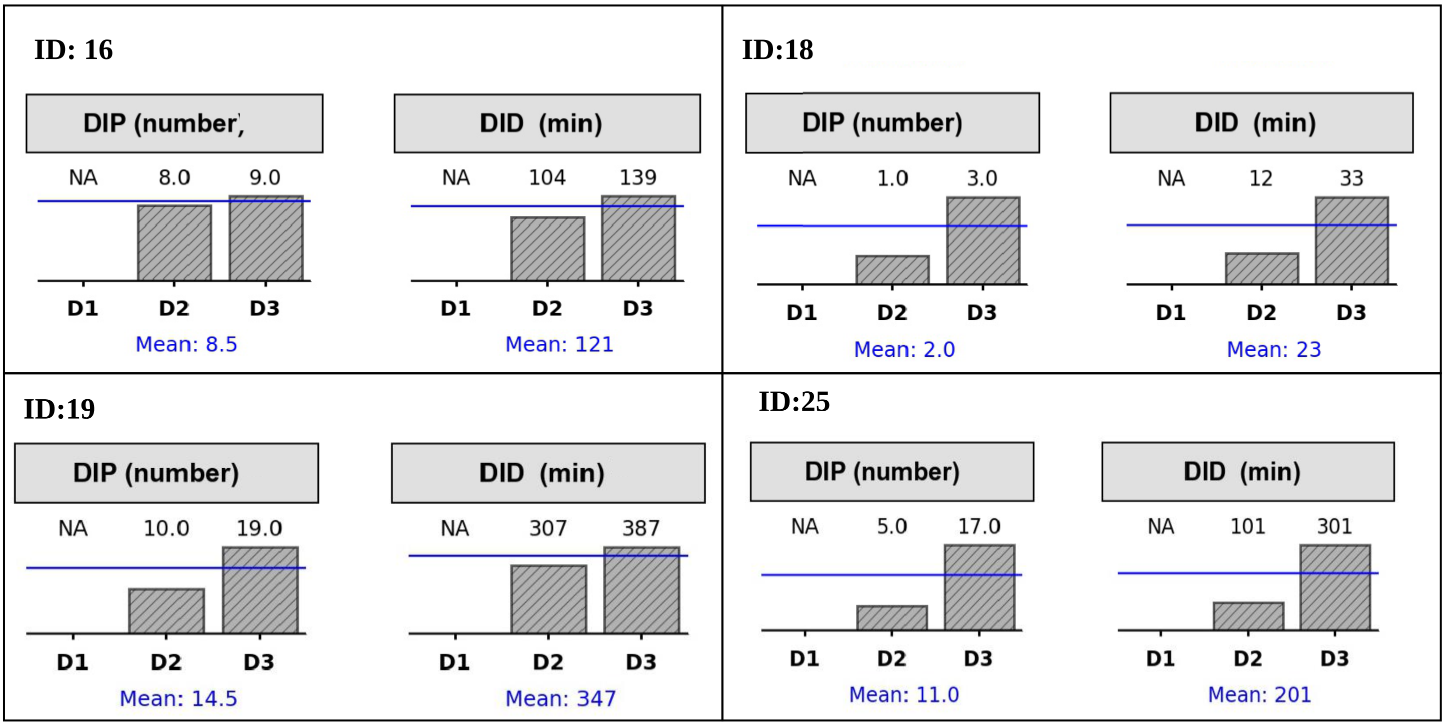


Figure 9- Results for periods of daytime immobility and duration of daytime immobility obtained by analysing accelerometer data from patients 16,18,19 and 25. Abbreviations: D1- day 1; D2- day 2; D3- day 3; N/A- not applicable DIP- diurnal immobility periods; DID- diurnal immobility duration.

## 4.5. Results of the Post-exam Questionnaire

After the image acquisition, the participants had to complete a post-exam questionnaire (answers shown in **Appendix N**), these results are present in Table 10.

With regard to the question "Did you understand the information given about the exam?" all participants said they understood the information given about the exam, Table 10. In both groups, the majority reported not feeling anxious, in CG 53.3% and EG 60.0%. Of those who reported feeling anxiety in the CG, 66.7% felt it during the exam. It is to be noted that in CG one patient answered that she felt anxiety but did not answer the follow-up question ("If yes, in which phase of the procedure?").

Table 10- Frequency analysis of the post-exam questionnaire.

| | CG<br>n (%) | EG<br>n (%) |
|---|---|---|
| **Understood the information given about the exam** | | |
| Yes | 15 (100) | 15 (100) |
| No | 0 (0.0) | 0 (0.0) |
| **Experience Anxiety** | | |
| Yes | 7 (46.7) | 6 (40.0) |
| No | 8 (53.3) | 9 (60.0) |
| **Anxiety in which phase of the procedure** | | |
| Before | 2 (33.3) | 2 (33.3) |
| During | 4 (66.7) | 2 (33.3) |
| After | 0 (0.0) | 0 (0.0) |
| Before, During, and After | 0 (0.0) | 2 (33.3) |
| **Music helps reduce anxiety** | | |
| Yes | | 5 (83.3) |
| No | | 1 (16.7) |
| **Right music to reduce anxiety** | | |
| Yes | | 14 (93.3) |
| No | | 1 (6.7) |

CG- control group; EG- experimental group.

In the EG, the percentages are equal between before, during and, before, during and after, 33.3%. It should be noted that two participants in this group reported feeling anxiety from the beginning of the procedure until they left the NM service. In both groups, no one reported feeling anxious after the exam.

Of the anxious patients, 83.3% said that listening to music help reduce anxiety. For all the EG, except one, the song that they heard was the right music style. This patient reported that music did not help to reduce anxiety and was not the right style, due to the pain in her legs she could not relax to the music.

Regarding patients that underwent the first-time NM exam 66.7% (n= 6) said that they were anxious, 60.0% before the exam, 11.1% during, and 11.1% before, during, and after.

## 4.6. Correlation of STAI results with other variables

In order to see if there is any correlation between the STAI results and the physiological measures, Table 11, we used the Spearman and Pearson correlation. A negative strong correlation between STAI pre-scan and diastolic BP was found in CG ($r_S$=-0.590; p=0.021) with statistical significance. The following significant correlations of moderate intensity in the negative direction were found with the STAI pre-scan: HR ($r_S$=-0.474; p=0.074) and RR ($r_S$=-0.382; p=0.159) with no statistically significant in CG. In the EG a positive moderate correlation between STAI post-scan and RR was found ($r_S$=0.545; p=0.036) with statistically significant. To correlate between a categorical and a scale variable we use eta correlation, Table 11. A moderate strength association between STAI pre-scan and academic education was found in pre-exam EG (r= 0.425) and between disease status in pre-exam CG (r= 0.394). This association also occurred between STAI post-scan and academic education CG after BS (r= 0.426), and between disease status in CG after BS (r= 0.504).

Table 11 – Correlations of STAI pre-scan and post-scan scores in the control and experimental group with the physiological measurements.

| | Correlation with STAI pre-scan | | Correlation with STAI post-scan | |
|---|---|---|---|---|
| **Variable** | CG before BS | EG before BS | CG after BS | EG after BS |
| Systolic BP | -0.282[a] | 0.238[b] | -0.148[b] | -0.180[a] |
| Diastolic BP | -0.590[a] | -0.032[b] | 0.069[b] | 0.050[a] |
| HR | -0.474[a] | -0.103[b] | -0.015[b] | -0.101[a] |
| RR | -0.382[a] | 0.204[b] | -0.182[b] | 0.545[a] |
| SpO2 | -0.193[a] | 0.100[a] | -0.179[b] | 0.059[a] |
| Age | -0.174[a] | -0.105[a] | 0.209[b] | -0.463[a] |
| Civil Status | 0.343[c] | 0.307[c] | 0.331 [c] | 0.315 [c] |
| Employment | 0.024[c] | 0.189[c] | 0.100[c] | 0.185[c] |
| Academic education | 0.073[c] | 0.425[c] | 0.426[c] | 0.222[c] |
| Physical activity | 0.087[c] | 0.205[c] | 0.123[c] | 0.179[c] |
| Depression or anxiety disorders | 0.039[c] | 0.116[c] | 0.031[c] | 0.214[c] |
| Hypertension or Antihypertensive therapy | 0.222[c] | 0.238[c] | 0.055[c] | 0.158[c] |
| Anxiolytic | 0.099 [c] | 0.130 [c] | 0.295 | 0.024 |
| Knows reason for BS | Yes, is a constant | 0.046[c] | Yes, is a constant | 0.623[c] |
| First BS | 0.047[c] | 0.223[c] | 0.222[c] | 0.195[c] |
| Previous NM | 0.199[c] | 0.024[c] | 0.096[c] | 0.032[c] |
| Disease status | 0.394[c] | 0.111[c] | 0.504[c] | 0.229[c] |

BS- bone scintigraphy; CG- control group; EG- experimental group; Systolic BP- systolic blood pressure; Diastolic BP- diastolic blood pressure; HR- heart rate; RR- respiratory rate; SpO2- Blood Oxygen Saturation.
a. Spearman correlation coefficient; b. Pearson correlation coefficient; c. Eta correlation.

# 5. Discussion

In this study, 96.7% of participants said they knew the reason for the exam. This value is superior to what is found in Grilo *et al.* (**2020**) with 90.4%. Our sample consisted of 80.0% of patients who had a previous NM exam (majority underwent BS previously) with only 9 participants who never had an NM exam, as such first time undergoing a BS. The contrary occurs in Grilo *et al.* **(2020)** wherein a sample of 42 patients for the BS group 33 had a BS for the first time. Thus, our study lacks participants with this characteristic but has a sample with more knowledge of why they underwent a BS.

The average age of patients in this study was 57.70±8.09 years, with a minimum of 45 years, and a maximum of 73 years. As for the level of education, most of them, 30.0% had primary education, 56.7% had secondary education, 10.0% had a bachelor's degree and 3.3% had a master's degree.

Concerning HR, we saw that EG values were higher than CG in the pre-exam to post-exam (pre-exam CG: 79.27±14.41; post-exam CG: 78.40±9.50; pre-exam EG: 83.93±13.80; post-exam EG: 86.87±13.12), with a slight decrease in CG and an increase in EG after BS (post-exam CG: 78.40±9.50; post-exam EG: 86.87±13.12). The opposite was found in Chen *et al.* (**2013**) a study that investigate the effects of music intervention on reducing pre-radiotherapy anxiety in oncology patients, where a significant decrease in heart rate from baseline to post-test was observed in both music and CG groups. In our study a statistically significance was detected regarding post-exam HR (post-exam HR: t= -2.024, p= 0.053. One of the reasons for the values in the EG being higher than in the CG may be because we are comparing the EG with a group that during image acquisition had no noise in the room, i.e., a place without stimuli, unlike the EG. It may have happened that in patients who listened to the music, the SNS was activated leading to an increase in HR. Although our aim to have patients listen to music was not to activate the SNS, this cannot be guaranteed. In EG we have more participants with depression and/or anxiety disorders and with hypertension or doing antihypertensive therapy than CG, this may be a factor that influences a higher HR average, as these patients may already have a higher HR baseline. Several studies also refer to an inconsistent phenomenon during music presentations where HR increases (by 1- 2 beats per minute) when compared to silence (Koelsch & Jancke, **2015**).

An unusual level of SpO2 was found post-exam in CG (93.13±1.85), some causes for lower SpO2 involve respiratory diseases, obesity, and smoking. To our best knowledge, our patients did not have respiratory diseases. Another explanation for this value could be that the patients were hyperventilation since increases in state anxiety can be accompanied by acute increases in RR and corresponding hypocapnia caused by hyperventilation (Giardino *et al.*, **2007**). Moreover, we observe an increase in RR in post-exam CG. This study was conducted during the COVID-19 pandemic, as such, we cannot ignore the hypothesis that the participants had COVID during data collection or that the lower SpO2 is a side effect of COVID-19 (Herrmann *et al.*, **2020**).

Regarding BP we observe that the mean values presented in both groups are considered elevated (>120/80mmHg), in Chen *et al.*, (**2013**) only systolic BP is elevated in both groups. Comparing our mean differences for physiological measures with Chen *et al.*, (**2013**) we see that we did not have a decrease in BP, HR, RR, and SpO2 variables after the exam as in their study, and that the differences between before and after are different from ours, but with a similar result for systolic BP difference in CG.

We observe that the STAI scores decrease in both groups after the scan but with no significant difference, this is not in line with Grilo *et al.* (**2020**) where a significant reduction in STAI scores between the pre-scan and post-scan STAI was shown ($t_{11}$= 2.450, p= 0.032, for the $^{99m}$Tc-HDP BS group). Comparing our results with Grilo *et al.* (**2020**) for differences in pre-scan STAI-S scores between patients undergoing the exam for the first time, and patients who had undergone it before were similar, no statistically significant differences were found in both studies. Furthermore, in our study, no statistically significant differences were also found in post-scan STAI-S scores between patients undergoing the exam for the first time and patients who had undergone it before. In Chen *et al.* (**2013**) no significant differences were found between groups in the pre-test STAI-S/STAI-T scores and vital signs before intervention. The same did not happen in our study, where a strong correlation between STAI pre-scan and diastolic BP in CG, and in EG a moderate correlation between STAI post-scan and RR with statistically significant was found.

A moderate strength association between STAI pre-exam and academic education was found in the pre-exam EG (r= 0.425) and between disease status in the pre-exam CG (r= 0.394), which means that academic education has an 18% effect on STAI pre-scan in the EG, and disease status has a 16% effect on STAI pre-scan in the CG. Between STAI post-exam and academic education in the post-exam CG (r= 0.426), and between disease status in post-exam CG (r= 0.504) a moderate strength association was found, that is academic education has an 18% and disease status has a 25% effect on STAI post-scan in CG.

Concerning the accelerometer data analysis, we found that EG is more stable in terms of invariability of the 24 hours rhythm between days (IS= 0.61±0.09), less fragmented in terms of rhythm (IV= 0.77±0.21), and has a more robust rhythm (RA= 0.92±0.05) than CG (IS= 0.57±0.13; IV= 0.94±0.18; RA= 0.89±0.08), that is EG has more quantity of activity and fewer frequency, and extent of transitions between rest and activity are fewer than CG. As for NTID, we see a big difference between CG (383.45±97.29) and EG (406.66± 80.48), with the latter group spending more time in immobility during the night than CG, that is, they have a more consistent sleep. The CG do not have as many periods of movement during the night (CG: NTMP= 9.80±4.25; EG: NTMP=26.21±75.72), however, they spend more time moving during this period than EG (CG: NTMD= 107.18±79.35; EG: NTMD= 82.86±48.27). Additionally, CG has more periods of sleeping during the day and a considerably longer duration of these periods than EG (CG: DIP= 10.18±6.41; DID= 208.27±145.84; EG: DIP= 6.07±4.61; DID= 121.88±132.47). When we compare the data by day, we found that the day before the exam participants have more sleepy periods during the day and stay in these periods for a longer duration compared with the other days (DIP: Day 2= 7.04±5.82; Day 3= 8.60±5.88; DID: Day 2= 139.75±133.70; Day 3= 179.01±155.19).

Regarding the physical activity energy expenditure, we found that our EG participants spend less time in sedentary activity than CG (EG: Sedentary: 1113.33±134.75; CG: 1186.88±140.61). The same goes for the sample where they spend more time in sedentary behaviour (1146.76±142.24) than any other physical activity energy expenditure, which is consistent with Thraen-Borowski *et al.*, (**2017**) where cancer survivors spend 62% of waking time in sedentary behaviour. In fact, Siobhan M. Phillips *et al*., (**2015**) found similar results for BC survivors, 66.4% of waking time in sedentary behaviour. This study also conclude that BC survivors registered more sedentary behaviour than non-cancer controls.

Patients reported that listening to music help reduce anxiety, in fact, 83.3% of the anxious participants in EG considered it to be useful with a similar result found in Santos *et al.* (**2018**).

In summary, the STAI and systolic BP decrease after the intervention. When we compared our results with other studies, we found that the use of music is associated with a decrease in anxiety. In the study described by Santos *et al.* (**2018**), there was a significant decrease in anxiety only in the group that listened to music, and an increase in anxiety in the CG. In the study Vogel *et al.* (**2012**), with music during the biodistribution phase combined with audio-visual media, anxiety decreased in both groups. In Lee *et al.*, (**2017**) the results show that patients in the EG had a significant reduction in state anxiety and HR, and in Chen *et al*., (**2013**) music therapy provided before radiation treatment decreases state-trait anxiety levels and systolic BP in oncology patients receiving radiotherapy.

# 6. Conclusions

Cancer is a disease that during its diagnosis/development leads to patients being submitted to multiple exams from various specialties. Often these exams are NM, which frightens the patient because of its name (nuclear), due to its complexity, duration, and the results that can change a patient's life or the course of treatment. As a result, patients tend to feel anxious when the NM exams are carried out, which may affect imaging acquisition and the duration of the exam. Hence, the medical staff has tried many methods to reduce the anxiety related to these exams. Such a method is to have the patients listen to music during the imaging acquisition, as a way to distract them and make them relax. This technique has been evaluated in exams such as PET, CT, and others but has not been used in BS. Therefore, this present study was developed, to test whether listening to music during a BS could help reduce anxiety in patients. To this end, several measurements were taken (BP, HR, RR, SpO2, and accelerometer).

Post-exam, we found that CG has higher mean values of BP and RR than EG. We have also observed an increase in systolic BP and a small increase in RR between the two moments of intervention for CG. As for EG a very small decrease in systolic BP and a small decrease in RR were detected. Regarding diastolic BP, this value decreases in CG and increases in EG after the exam. The mean values obtained for BP are considered elevated (>120/80mmHg) and the RR normal. In regards to HR average values obtained were normal, with EG values being higher than CG before and after the exam, a slight decrease in values in CG, and an increase in EG after BS was seen. For this variable, statistically significant differences were detected between CG and post-exam EG. For SpO2 an abnormal level mean value was identified in post-exam CG, 93.13%, the most likely cause of this value occurring is the patients' hyperventilation, this is supported by the fact that RR increases in this group after the exam. Statistically significant differences were found between CG and post-exam EG SpO2, as well as a negative strong correlation between STAI pre-scan and diastolic BP in CG, and a positive moderate correlation between STAI post-scan and RR in EG with statistically significant.

The STAI scores decrease in both groups after the scan but with no statistically significant differences. As for the accelerometer data, we found that the day before the exam participants have more sleepy periods during the day and stay in these periods for a longer duration compared with the other days and that our participants spend more time in sedentary behaviour.

In conclusion, the current study suggests that listening to music during BS seems to reduce patients' anxiety considering that STAI scores and systolic BP in EG decrease after the exam.

## 6.1. Limitations

We encountered several limitations during this study. Firstly, our sample size was small and only included patients related to one NM department. Secondly, self-reporting questionnaires are the most common methodology for studying subjects such as anxiety and patient experience, but they are not without issues. The patients' understanding of the items is one of the main apprehensions. In our study, all patients were told that during the completion of the questions they could clarify any doubts with the researcher present in the same room. However, this did not prevent interpretations emerging that differed from those of the researcher. Thirdly, even though the most used method for measuring RR is simply counting the number of breaths for one minute, we cannot overrule subjective error from the researcher. Fourth, measuring psychological measures post-exam, after moving the patient into a resting room may have influenced some results. Fifth, as we sent documents and the accelerometer to patients' homes patients may have felt anxiety about participating in the study. Finally, on the days when the wrist accelerometer was recording data, it was not always possible to obtain 22 recording hours to be able to treat the data afterwards.

## 6.2. Future work

For future work, a bigger sample from different NM departments with a greater representation of patients undergoing a BS for the first time should be used, as well as a different method to measure RR. The post-exam physiological measurements should be taken before lifting the patient from the equipment, to check whether the post-exam measurements when collected in a resting room affect the result and by how much. It also may be beneficial to ask the patients in the pre-exam questionnaire if they feel anxious at that moment, for association with the post-exam question “Did you feel anxiety before, during, or after the exam? ”. With regard to recording wrist accelerometer data, it may be of interest to record for a longer period, to assess, whether after leaving the hospital patients still feel anxious and to evaluate physical activity between pre-exam and post-exam. Additionally, at the time of the data recording period by the accelerometers, it would be interesting to collect at the same time the physiological measurements, in order to, check if there is any correlation between DIP and DID with the physiological measurements.

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## **Appendix A:** Brief text explaining the project

Exmo (a) Senhor(a)

Maria Boal, estudante do Mestrado de Engenharia Biomédica do Instituto Superior de Engenharia de Lisboa/Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa, ISEL/ESTeSL/IPL sob a orientação de Lina da Conceição Capela de Oliveira Vieira, docente da ESTeSL/IPL, em colaboração com o Serviço de Medicina Nuclear do Hospital Particular de Almada, encontra-se a desenvolver o trabalho de final de Mestrado, subordinado ao tema "*Efeitos da música em pacientes que realizam Cintigrafias Ósseas*". Pretende-se contribuir para um melhor conhecimento sobre este tema, sendo necessário, para tal, que alguns participantes, ouvirem uma música, pré-selecionada, durante a aquisição das imagens de Cintigrafia Óssea.

É neste âmbito, e caso seja do seu agrado, que venho junto de V. Ex.ª solicitar a sua autorização, para receber mais informação e decidir se pretende participar neste estudo.

Mais informo, que caso aceite participar neste estudo, não será sujeito a qualquer dose extra de radiação, nem a nenhum efeito secundário. Será apenas submetido aos exames que o seu médico solicitou para esclarecimento da sua condição clínica.

Apenas terão que usar um acelerómetro de pulso durante 3 dias (3 dias antes do exame), e responder a um questionário antes e outro após o exame CO, no serviço de Medicina Nuclear. Todos os participantes receberão a mesma informação oral sobre o exame. Para além disto, alguns pacientes serão selecionados para ouvir uma música pré-selecionada, durante a aquisição das imagens de CO.

Lisboa, 11 dezembro de 2020

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|---|---|
| (Maria Boal)<br>Estudante do Mestrado Engenharia Biomédica<br>ESTeSL/IPL | (Lina Vieira)<br>Prof.ª Coordenadora |

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Eu;______________________________________________________________ compreendi todas a explicações que me foram dadas e:

_______Aceito receber mais informação

_______Não aceito receber mais informação

Em caso de ter respondido que aceita receber mais informação e decidir se irá participar no estudo, agradecemos que nos indique:

N.º telemóvel ______________________

Endereço Eletrónico (e-mail) ________________________
Morada:

Estes contactos serão apenas utilizados pela estudante de Mestrado Maria Boal e exclusivamente para divulgação do estudo, envio de questionários e/ou pulseira a usar durante um período de tempo de 4 dias (3 dias antes do exame e durante o dia do exame).

# **Appendix B:** Informed consent

## CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO PARA PARTICIPAÇÃO EM INVESTIGAÇÃO

**de acordo com a Declaração de Helsínquia[1] e a Convenção de Oviedo[2]**

*Por favor, leia com atenção a seguinte informação. Se achar que algo está incorreto ou que não está claro, não hesite em solicitar mais informações. Se concorda com a proposta que lhe foi feita, queira assinar este documento.*

**Título do estudo:** "*Efeitos da música em pacientes que realizam Cintigrafias Ósseas*"

**Enquadramento**: O atual trabalho de investigação, a ser desenvolvido no Hospital Particular de Almada, insere-se num estudo que decorre no âmbito do Mestrado de Engenharia Biomédica do Instituto Superior de Engenharia/Escola Superior de Tecnologia de Saúde de Lisboa – Instituto Politécnico de Lisboa, sob orientação da Professora Doutora Lina da Conceição Capela de Oliveira Vieira e do Professor Doutor Tiago Guerreiro.

**Explicação do estudo**: O estudo tem como principal objetivo investigar o efeito de música no controlo de parâmetros fisiológicos, em pacientes com cancro da mama, durante a aquisição de exames de cintigrafia óssea. Pretende-se contribuir para um melhor conhecimento sobre este tema, sendo necessário, para tal, que alguns participantes, quando solicitado, oiçam música pré-selecionada, durante a aquisição das imagens de CO.

**Finalidade do tratamento de dados pessoais**: Serão recolhidos os seguintes dados pessoais: género, idade, habilitações académicas, situação laboral. Estes dados destinam-se à caraterização geral da amostra do estudo. Será ainda solicitado o endereço de correio eletrónico, morada e contacto telefónico para que, seja enviada o Acelerómetro de pulso, e quatro dias anteriores ao exame, seja possível relembrar para colocar o Acelerómetro de pulso. Para além disso, no dia do exame, será recolhida a tensão arterial, número de batimentos por minuto, frequência respiratória, nível de oxigénio medido no sangue e quantidade de suor produzido nas mãos, assim como informações relacionadas com o nível de ansiedade recolhida através dos questionários STAI.
Os dados recolhidos são para uso exclusivo do presente estudo, não existindo quaisquer interesses financeiros a motivar o estudo, nem transferência dos seus dados para outros investigadores que não integrem o projeto.

**Confidencialidade, anonimato e conservação dos dados**: A confidencialidade e anonimato dos seus dados serão garantidos. A identificação far-se-á por um código e, após análise de toda a informação recolhida, e divulgação pela comunidade científica dos resultados gerais, os dados serão eliminados.

**Encarregado da Proteção de Dados**: Os contactos do Encarregado da Proteção de Dados (EPD) do presente estudo são: Profª Lina Vieira; lina.vieira@estesl.ipl.pt;

**Os seus direitos**: Pode exercer o seu direito de acesso aos dados pessoais, bem como a sua retificação ou o seu apagamento, e a limitação do tratamento, ou o direito de se opor ao tratamento enviando um email para _lina.vieira@estesl.ipl.pt.

**Reclamação à autoridade de controlo**: Enquanto titular dos dados pessoais, tem o direito de apresentar reclamação junto da Comissão Nacional de Proteção de Dados (CNPD), autoridade de controlo em Portugal.

[1] http://portal.arsnorte.min-saude.pt/portal/page/portal/ARSNorte/Comiss%C3%A3o%20de%20%C3%89tica/Ficheiros/Declaracao_Helsinquia_2008.pdf

[2] http://dre.pt/pdf1sdip/2001/01/002A00/00140036.pdf

**Condições e financiamento**: A sua participação é voluntária, não existindo nenhuma contrapartida financeira ou de outra natureza, à sua participação. Em qualquer momento, poderá livremente recusar ou interromper a participação no estudo, sem qualquer tipo de penalização por este facto.

Em nome da equipa de investigação do projeto, manifesto os nossos agradecimentos pela sua participação e a nossa disponibilidade para quaisquer esclarecimentos adicionais.

**Assinaturas**:

… … … … … … … …... … … … …... … … … … … … … … … … … …… … … … … … …... … … … …... … … … … … … … … … … …

____________________________________ - Investigador que lhe apresentou o projeto, em nome de:

Maria Boal – Estudante de Mestrado em Engenharia Biomédica – Instituto Superior de Engenharia de Lisboa/ Escola Superior de Tecnologia da Saúde de Lisboa – Instituto Politécnico de Lisboa. Contactos telefónicos: 911038696
Lina Oliveira Vieira - Professora Coordenadora da Escola Superior de Tecnologia da Saúde de Lisboa. Contactos Telefónicos: 913774980.

-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-

*Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pelas pessoas que acima assinam. Foi-me garantida a possibilidade de, em qualquer altura, recusar participar neste estudo sem qualquer tipo de consequências. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando em que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas pelos investigadores.*

Nome: … … … … … … … …... … … … …... … … … … … … … … … … … …… … … … … … …... … … … …... … … … … … … … …
Assinatura: … … … … … … … …... … … … … ... … … … … … … … … … … … … …
Data: …… /…… /………..

SE NÃO FOR O PRÓPRIO A ASSINAR POR IDADE OU INCAPACIDADE
(se o menor tiver discernimento deve <u>também</u> assinar em cima, se consentir)
NOME: … … … … … … … … … … … … … … … … … … … … … … … … … … … … … … …
BI/CD Nº: .......................................... DATA OU VALIDADE ….. /..… /…....
GRAU DE PARENTESCO OU TIPO DE REPRESENTAÇÃO: ....................................................
ASSINATURA … … … … … … … … … … … … … … … … … … … … … … … … … … … … … …

**ESTE DOCUMENTO É COMPOSTO DE 2 PÁGINAS E FEITO EM DUPLICADO: UMA VIA PARA O/A INVESTIGADOR/A, OUTRA PARA A PESSOA QUE CONSENTE**

# **Appendix C:** Pre-exam questionnaire

**Questionário pré-exame**

**ID do paciente:___________** **Grupo: _________**

1. Idade:_____(anos)

2. Qual é o seu estado civil?

☐ Solteira ☐ Casada ☐ Divorciada ☐ Viúva ☐ Separada

3. Possui um emprego?

☐ Sim ☐ Não

4. Formação académica

☐ Ensino Básico

☐ Ensino Secundário

☐ Licenciatura

☐ Mestrado

☐ Doutoramento

5. Praticou atividade física nos 3 dias antecedentes quando utilizava a pulseira?

☐ Sim ☐ Não

6. Sofre de depressão ou distúrbio de ansiedade?

☐ Sim ☐ Não

Se sim, diga qual: _____________________

7. É hipertensa ou faz terapêutica anti-hipertensora?

☐ Sim ☐ Não

8. Tomou algum ansiolítico/calmante antes da realização do exame?

☐ Sim ☐ Não

9. Sabe a razão pela qual vêm realizar a Cintigrafia Óssea?

☐ Sim ☐ Não

Se sim, diga qual: ______________________

10. É a primeira vez que realiza um exame de Medicina Nuclear?

☐ Sim ☐ Não

Se não, diga qual realizou: ________________

# **Appendix D:** Pre-exam STAI Questionnaire

**Questionário STAI – Antes da aquisição de imagens**

(Spielberger, Gorsuch & Lushene, 1983; versão portuguesa Silva, 2003)

**ID do paciente: ________** **Grupo: _____** **Data ____/____/____**

**Instruções**: Abaixo encontra uma série de afirmações que as pessoas costumam usar para se descreverem a si próprias. Leia cada frase cuidadosamente e de seguida **assinale o círculo apropriado** à direita, indicando como se sente **agora**, neste preciso **momento**. Não há respostas certas nem erradas. Não gaste demasiado tempo em cada frase, dê a resposta que melhor parece descrever como se sente agora.

**1 - Nada 2 – Um pouco 3 - Moderadamente 4 – Muito**

| | | | | |
|---|---|---|---|---|
| 1. Sinto-me esgotado……………………………………………………………......... | 1 | 2 | 3 | 4 |
| 2. Sinto-me à vontade………………………………………………………………… | 1 | 2 | 3 | 4 |
| 3. Presentemente ando preocupado com desgraças que possam vir a acontecer……………………………………………………………………………………… | 1 | 2 | 3 | 4 |
| 4. Estou descansado…………………………………………………………………… | 1 | 2 | 3 | 4 |
| 5. Sinto-me nervoso…………………………………………………………………… | 1 | 2 | 3 | 4 |
| 6. Estou descontraído………………………………………………………………… | 1 | 2 | 3 | 4 |
| 7. Sinto-me contente…………………………………………………………………… | 1 | 2 | 3 | 4 |
| 8. Sinto-me uma pessoa estável………………………………………………………… | 1 | 2 | 3 | 4 |

# **Appendix E:** Post-exam STAI Questionnaire

**Questionário STAI – Após a aquisição de imagens**
(Spielberger, Gorsuch & Lushene, 1983; versão portuguesa Silva, 2003)

**ID do paciente: ________** **Grupo: _____** **Data ____/____/____**

**Instruções**: Abaixo encontra uma série de afirmações que as pessoas costumam usar para se descreverem a si próprias. Leia cada frase cuidadosamente e de seguida **assinale o círculo apropriado** à direita, indicando como se sente **agora**, neste preciso **momento**. Não há respostas certas nem erradas. Não gaste demasiado tempo em cada frase, dê a resposta que melhor parece descrever como se sente agora.

**1 - Nada** **2 – Um pouco** **3 - Moderadamente** **4 – Muito**

| | | | | |
|---|---|---|---|---|
| 1. Sinto-me esgotado………………………………………………………......... | 1 | 2 | 3 | 4 |
| 2. Sinto-me à vontade………………………………………………………… | 1 | 2 | 3 | 4 |
| 3. Presentemente ando preocupado com desgraças que possam vir a acontecer……………………………………………………………………………… | 1 | 2 | 3 | 4 |
| 4. Estou descansado………………………………………………………………… | 1 | 2 | 3 | 4 |
| 5. Sinto-me nervoso………………………………………………………………… | 1 | 2 | 3 | 4 |
| 6. Estou descontraído……………………………………………………………… | 1 | 2 | 3 | 4 |
| 7. Sinto-me contente………………………………………………………………… | 1 | 2 | 3 | 4 |
| 8. Sinto-me uma pessoa estável………………………………………………… | 1 | 2 | 3 | 4 |

# **Appendix F:** Post-exam questionnaire

**Questionário após a realização do exame**

**ID do paciente:**___________ **Grupo:** _________

1. Compreendeu a informação dada sobre o exame?

☐ Sim ☐ Não

2. Sentiu ansiedade antes, durante ou após o exame?

☐ Sim ☐ Não (se respondeu **Não**, passe para a questão 4 se ouviu música durante o exame)

Se sim, indique em que fase (antes, durante ou após): ___________________________

**(Se ouviu música durante o exame Cintigrafia Óssea, responda as questões 3 e 4)**

3. A música ouvida durante o exame foi útil para reduzir o seu grau de ansiedade?

☐ Sim ☐ Não

4. Considera a música que lhe fizemos ouvir a indicada para reduzir a ansiedade?

☐ Sim ☐ Não

Se não, diga porque: ___________________________________________

# **Appendix G:** Opinion of the Ethics Committee of the ESTeSL

REFERÊNCIA INTERNA DO PROJETO: CE-ESTeSL-Nº.96 -2020 - Maria Ferreira Boal

TÍTULO DO DE PROJETO: Efeitos da música em pacientes que realizam Cintigrafias Ósseas TIPO DE PROJETO/ESTUDO: Mestrado em Engenharia Biomedica

INVESTIGADOR/A PRINCIPAL: Maria Ferreira Boal

ORIENTADORES: Lina Vieira

INSTITUIÇÃO PROMOTORA: Escola Superior de Tecnologia da Saúde de Lisboa-IPL

Exma. Senhora Professora Doutora Lina Vieira

Exma. Senhora Dra. Maria Ferreira Boal, estudante mestrado

Após os esclarecimentos de 24 de maio, a Comissão de Ética da Escola Superior de Tecnologia da Saúde de Lisboa (CE-ESTeSL) decidiu por unanimidade a emissão de parecer favorável com a recomendação que todos os participantes mesmo os que não ouvem música nesses dias tem de ser informados da inclusão no estudo.

Lembramos ainda que todos os estudos que envolvem a autorização dos participantes e a recolha de amostras e dados anonimizados e/ou codificados têm de cumprir com o estabelecido no Regulamento Geral sobre a Proteção de Dados de 27 de abril de 2016.

Por último, solicita-se também que, ao abrigo do artº 19 da Lei 21/2014 de 16 de abril e do disposto no nº23 da atual versão da Declaração de Helsínquia, dê igualmente conhecimento à CE-ESTeSL do relatório final com as conclusões do estudo, de eventuais alterações ao protocolo de investigação e demais informações tidas por relevantes.

Aproveitamos ainda para desejar o maior sucesso no desenvolvimento deste trabalho.

Com os melhores cumprimentos

Rute Borrego

## **Appendix H:** Protocol followed by *NuclearMed* in bone scintigraphy

**PROCEDIMENTO PARA**

**REALIZAÇÃO DE EXAME**

| **Revisão:** | **Data:** |
| --- | --- |
| 00 | 18/6/2005 |
| 01 | 07/07/2005 |
| 02 | 05/06/2013 |
| 03 | 13/01/2017 |
| 04 | 22/08/2019 |

<table>
<tr><td rowspan="3">Lista de Distribuição:<br><br>- Técnicos MN<br><br>- Médicos MN</td><td>Elaborado por:<br>Edgar Lemos Pereira</td></tr>
<tr><td>Revisto por:<br>Luís Oliveira; Marco Fernandes; Ana Mota</td></tr>
<tr><td>Observações:</td></tr>
</table>

## 1. Cintigrafia Óssea de Corpo Inteiro - E601

| | | |
|---|---|---|
| **Preparação do cliente:** | Sem preparação | |
| **Radiofármaco:** | HDP ou HMDP ou outro difosfonato marcado com 99mTc | |
| **Via e local de Administração:** | Endovenosa<br>Local contralateral à lesão (caso se aplique) | |
| **Dose administrada:** | 740 MBq | LST06 |
| **Informação a dar ao cliente:** | Hidratação frequente<br>Micção frequente<br>Duração total de exame 3 a 4h | |
| **Tempo para obtenção de imagens:** | No mínimo 1h30 após a administração do radiofármaco | |
| **Protocolo de aquisição:** | Protocolo da Câmara Gama - Óssea Tardia<br>Indicação do Médico Especialista | |
| **Posicionamento do cliente:** | No estudo de corpo inteiro, decúbito dorsal com os braços ao longo do corpo e pés em rotação interna. Deve ser utilizada a banda larga de tecido para suporte e estabilização dos membros superiores (zona do cotovelo) e maior conforto do cliente. Deve também ser ponderada a colocação de uma almofada nos membros inferiores (fossa popliteia) para maior conforto do cliente.<br>Outro posicionamento pode ser ponderado de acordo com as limitações físicas do cliente bem como indicação médica.<br>Todas as imagens estáticas devem ser adquiridas colimando a região anatómica que se pretende visualizar, na posição mais confortável possível para o cliente. | |
| **Tempo duração de imagens:** | 20-30 minutos. Acresce 20-30 minutos, caso seja adquirido estudo SPECT. | |
| **Ficha Clínica:** | Sistema informático (Aplicação "*Gestão de Processos Clínicos*"/<br>Preenchimento em papel em caso de falha do sistema. | MOD13 |
| **Cuidados Especiais:** | Deve ser verificada e confirmada a identidade do cliente com o primeiro e ultimo nome e se necessário a data de nascimento.<br>É obrigatória a confirmação da prescrição médica bem como a indicação clínica.<br>Todos os clientes devem assinar o consentimento informado e todas as mulheres em idade fértil devem garantir a não gravidez e amamentação.<br>Retirar objectos radiopacos da zona de interesse.<br>Urinar imediatamente antes da aquisição das imagens.<br>Não aplicar hidratação especial em doentes com restrição hídrica (Insuficiente renal crónico e programa de hemodiálise).<br>Confirmar a quando da alta do cliente, a data da consulta bem como forma de entrega do resultado do exame | |

**Appendix I:** Table of pre-exam questionnaire responses

| | ID | 1. | 2. | 3. | 4. | 5. | 6. | 6.1. | 7. | 8. | 9. | 9.1. | 10. | 10.1 | Disease status |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 48 | Married | Yes | Secondary Education | No | No | N/A | No | No | Yes | Breast cancer | No | BS | |
| | 3 | 47 | Divorced | Yes | Master's Degree | No | No | N/A | No | No | Yes | Breast tumour staging | No | MRI | Initial staging |
| | 5 | 45 | Single | Yes | Primary Education | Yes | No | N/A | No | No | Yes | Bone pain | No | BS | |
| | 7 | 60 | Married | Yes | Secondary Education | No | No | N/A | No | No | Yes | Breast cancer | No | Lymphoscintigraphy | Treatment phase (chemotherapy) |
| | 9 | 47 | Married | Yes | Secondary Education | Yes | Yes | Anxiety | No | No | Yes | Bone pain | No | BS | Follow up |
| CG | 11 | 66 | Widow | No | Primary Education | No | No | N/A | Yes | No | Yes | Breast tumour staging | Yes | N/A | Initial staging |
| | 13 | 54 | Divorced | No | Secondary Education | No | No | N/A | No | No | Yes | Breast cancer | No | BS | Follow up |
| | 15 | 52 | Married | Yes | Secondary Education | No | No | N/A | No | No | Yes | Breast cancer | No | BS | Follow up |
| | 17 | 61 | Single | No | Secondary Education | No | Yes | Depression | No | No | Yes | Screening for metastases | No | BS | Treatment phase (hormonal) |
| | 19 | 73 | Married | No | Primary Education | No | No | N/A | Yes | No | Yes | Breast cancer | No | BS | Treatment phase (chemotherapy) |
| | 21 | 49 | Married | Yes | Bachelor’s degree | No | No | N/A | No | No | Yes | Screening for metastases | No | BS | Treatment phase (chemotherapy) |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 23 | 55 | Married | Yes | Secondary Education | No | No | N/A | No | No | Yes | Bone lesion | No | BS | Treatment phase (radiotherapy) |
| | 25 | 73 | Married | No | Secondary Education | No | No | N/A | Yes | Yes | Yes | Breast cancer | Yes | N/A | Treatment phase (hormonal) |
| | 27 | 64 | Married | Yes | Bachelor’s degree | Yes | Yes | Anxiety and Panic Attack | Yes | No | Yes | Breast cancer | No | Bone Densitometry | Follow up |
| | 29 | 65 | Married | No | Primary Education | No | No | N/A | No | No | Yes | Bone pain | No | BS | Treatment phase (hormonal) |
| | 2 | 56 | Married | Yes | Secondary Education | No | Yes | Anxiety | No | Yes | Yes | Screening for metastases | No | BS | |
| | 4 | 58 | Married | Yes | Secondary Education | No | No | N/A | No | No | Yes | Generalised pain (breast cancer) | No | BS | |
| | 8 | 58 | Married | No | Secondary Education | No | No | N/A | Yes | No | Yes | Generalised pain (breast cancer) | No | BS | Follow up |
| | 10 | 55 | Married | Yes | Secondary Education | Yes | Yes | Anxiety | Yes | No | Yes | Breast cancer | No | BS | Follow up |
| EG | 12 | 56 | Married | No | Primary Education | No | Yes | Anxiety | Yes | No | Yes | Generalised pain (breast cancer) | No | BS | Follow up |
| | 14 | 72 | Married | No | Primary Education | No | No | N/A | Yes | No | Yes | To complete hormone therapy | No | BS | Follow up |
| | 16 | 60 | Separated | Yes | Primary Education | No | Yes | Depression | No | Yes | Yes | Breast cancer | Yes | N/A | Treatment phase (chemotherapy) |
| | 18 | 48 | Married | Yes | Secondary Education | Yes | No | N/A | No | No | Yes | Spinal cysts | Yes | N/A | Follow up |
| | 20 | 59 | Divorced | Yes | Secondary Education | No | Yes | Depression | No | Yes | No | N/A | No | BS | Follow up |
| | 22 | 45 | Single | No | Secondary Education | No | Yes | Depression and Anxiety and Panic Attack | No | Yes | Yes | Screening for metastases | No | BS | Follow up |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 24 | 61 | Widow | Yes | Secondary Education | No | No | N/A | No | No | Yes | Screening for metastases | No | BS | Treatment phase (hormonal) |
| 26 | 62 | Divorced | Yes | Bachelor's degree | No | No | N/A | No | No | Yes | Pain in legs | No | BS | Follow up |
| 28 | 67 | Married | No | Secondary Education | No | No | N/A | Yes | Yes | Yes | Pain in legs | No | Lymphoscinti graphy | Treatment phase (hormonal) |
| 30 | 62 | Divorced | Yes | Primary Education | Yes | No | N/A | Yes | Yes | Yes | Breast cancer | Yes | N/A | Treatment phase (hormonal) |
| 32 | 53 | Married | Yes | Primary Education | No | No | N/A | No | Yes | Yes | Breast cancer | Yes | N/A | Treatment phase (chemotherapy) |

1.Age (years); 2. Civil Status; 3. Job; 4. Academic Education; 5. Physical activity; 6. Depression or anxiety disorders; 6.1. If yes, say which; 7. Hypertension or Antihypertensive Therapy; 8. Anxiolytic before the exam;9. Do you know why you come for a BS; 9.1. If yes, say which bone scintigraphy; 10. First Time performing Nuclear Medicine exam; 10.1. If no say which nuclear medicine exam; CG- Control group; EG- Experimental group; N/A- Not applicable; BS- Bone scintigraphy; MRI- Magnetic resonance imaging.

# **Appendix J:** Table of pre-exam physiological measurements

| Group | ID | Systolic blood pressure (mmHg) | Diastolic blood pressure (mmHg) | Heart Rate (beats/minute) | Respiratory Rate (breaths/minute) | Blood oxygen saturation (%) |
|---|---|---|---|---|---|---|
| CG | 1 | 127 | 69 | 65 | 13 | 98 |
| | 3 | 120 | 85 | 80 | 16 | 96 |
| | 5 | 133 | 85 | 79 | 18 | 95 |
| | 7 | 145 | 95 | 90 | 14 | 96 |
| | 9 | 104 | 77 | 73 | 15 | 99 |
| | 11 | 183 | 102 | 64 | 19 | 98 |
| | 13 | 110 | 75 | 65 | 12 | 99 |
| | 15 | 136 | 100 | 112 | 14 | 99 |
| | 17 | 107 | 71 | 102 | 13 | 96 |
| | 19 | 149 | 95 | 75 | 14 | 99 |
| | 21 | 141 | 94 | 87 | 14 | 99 |
| | 23 | 132 | 80 | 71 | 18 | 94 |
| | 25 | 128 | 68 | 66 | 14 | 97 |
| | 27 | 156 | 82 | 90 | 13 | 96 |
| | 29 | 140 | 68 | 70 | 12 | 93 |
| EG | 2 | 138 | 58 | 99 | 20 | 97 |
| | 4 | 131 | 79 | 79 | 17 | 97 |
| | 6 | 133 | 88 | 83 | 17 | 98 |
| | 8 | 129 | 70 | 68 | 17 | 99 |
| | 10 | 151 | 94 | 61 | 12 | 99 |
| | 12 | 147 | 89 | 83 | 15 | 95 |
| | 14 | 103 | 69 | 95 | 10 | 98 |
| | 16 | 116 | 77 | 69 | 10 | 95 |
| | 18 | 136 | 103 | 110 | 16 | 98 |

| | | | | | |
|---|---|---|---|---|---|
| 20 | 100 | 66 | 92 | 16 | 99 |
| 22 | 143 | 77 | 88 | 14 | 97 |
| 24 | 136 | 78 | 89 | 16 | 99 |
| 26 | 158 | 80 | 98 | 12 | 95 |
| 28 | 140 | 72 | 77 | 13 | 98 |
| 30 | 144 | 80 | 68 | 14 | 96 |

CG- Control group; EG- Experimental group.

# **Appendix K:** Table of post-exam physiological measures

| Group | ID | Systolic blood pressure (mmHg) | Diastolic blood pressure (mmHg) | Heart Rate (beats/minute) | Respiratory Rate (breaths/minute) | Blood oxygen saturation (%) |
|---|---|---|---|---|---|---|
| CG | 1 | 122 | 60 | 70 | 14 | 98 |
| | 3 | 117 | 83 | 73 | 14 | 94 |
| | 5 | 157 | 91 | 75 | 20 | 98 |
| | 7 | 153 | 91 | 93 | 15 | 98 |
| | 9 | 122 | 73 | 75 | 19 | 94 |
| | 11 | 177 | 92 | 79 | 18 | 98 |
| | 13 | 113 | 76 | 72 | 14 | 96 |
| | 15 | 142 | 96 | 72 | 14 | 95 |
| | 17 | 135 | 91 | 98 | 13 | 96 |
| | 19 | 147 | 83 | 73 | 14 | 99 |
| | 21 | 125 | 87 | 81 | 15 | 97 |
| | 23 | 114 | 72 | 91 | 20 | 96 |
| | 25 | 138 | 78 | 73 | 19 | 96 |
| | 27 | 156 | 79 | 86 | 15 | 94 |
| | 29 | 119 | 73 | 65 | 9 | 93 |
| EG | 2 | 135 | 82 | 86 | 14 | 97 |
| | 4 | 137 | 87 | 67 | 18 | 99 |
| | 6 | 136 | 97 | 103 | 18 | 98 |
| | 8 | 131 | 61 | 76 | 14 | 99 |
| | 10 | 137 | 83 | 75 | 15 | 98 |
| | 12 | 130 | 78 | 83 | 12 | 96 |
| | 14 | 138 | 79 | 88 | 9 | 99 |
| | 16 | 108 | 78 | 73 | 12 | 98 |
| | 18 | 161 | 113 | 111 | 14 | 96 |
| | 20 | 104 | 72 | 105 | 17 | 98 |

| | | | | | |
|---|---|---|---|---|---|
| 22 | 144 | 72 | 96 | 15 | 94 |
| 24 | 135 | 81 | 97 | 16 | 98 |
| 26 | 135 | 73 | 75 | 8 | 99 |
| 28 | 131 | 70 | 88 | 15 | 99 |
| 30 | 138 | 73 | 80 | 16 | 99 |

CG- Control group; EG- Experimental group.

# **Appendix L:** Table of pre-exam STAI responses

| Group | ID | I feel exhausted | I feel at ease | At the moment I'm worried about the misfortune that might happen | I'm rested | I feel nervous | I am relaxed | I feel happy | I feel stable | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| CG | 1 | 3 | 4 | 4 | 4 | 4 | 4 | 3 | 4 | 30 |
| | 3 | 2 | 4 | 3 | 2 | 2 | 3 | 2 | 4 | 22 |
| | 5 | 1 | 4 | 2 | 2 | 1 | 2 | 3 | 3 | 18 |
| | 7 | 2 | 3 | 3 | 2 | 2 | 2 | 1 | 4 | 19 |
| | 9 | 1 | 4 | 2 | 3 | 2 | 4 | 3 | 3 | 22 |
| | 11 | 4 | 2 | 3 | 2 | 2 | 2 | 1 | 4 | 20 |
| | 13 | 3 | 3 | 2 | 3 | 3 | 2 | 3 | 3 | 22 |
| | 15 | 1 | 2 | 3 | 2 | 1 | 2 | 3 | 3 | 17 |
| | 17 | 1 | 4 | 1 | 3 | 3 | 2 | 1 | 4 | 19 |
| | 19 | 1 | 4 | 2 | 4 | 1 | 2 | 2 | 2 | 18 |
| | 21 | 3 | 2 | 2 | 3 | 3 | 2 | 3 | 3 | 21 |
| | 23 | 2 | 4 | 1 | 2 | 1 | 4 | 3 | 4 | 21 |
| | 25 | 1 | 3 | 4 | 3 | 3 | 3 | 1 | 2 | 20 |
| | 27 | 1 | 3 | 4 | 2 | 3 | 3 | 3 | 3 | 22 |
| | 29 | 4 | 3 | 4 | 4 | 3 | 3 | 4 | 3 | 28 |
| EG | 2 | 2 | 4 | 3 | 4 | 1 | 4 | 3 | 4 | 25 |
| | 4 | 1 | 4 | 1 | 4 | 1 | 4 | 4 | 4 | 23 |
| | 6 | 1 | 4 | 3 | 4 | 1 | 1 | 3 | 3 | 20 |
| | 8 | 2 | 3 | 1 | 2 | 2 | 2 | 3 | 3 | 18 |
| | 10 | 2 | 4 | 3 | 4 | 4 | 4 | 3 | 3 | 27 |
| | 12 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 9 |
| | 14 | 2 | 2 | 3 | 3 | 3 | 1 | 1 | 1 | 16 |
| | 16 | 4 | 3 | 2 | 1 | 2 | 3 | 2 | 2 | 19 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 18 | 4 | 2 | 3 | 2 | 2 | 3 | 1 | 2 | 19 |
| 20 | 4 | 2 | 4 | 1 | 2 | 1 | 2 | 1 | 17 |
| 22 | 1 | 3 | 2 | 3 | 3 | 3 | 2 | 4 | 21 |
| 24 | 1 | 4 | 3 | 4 | 3 | 3 | 3 | 4 | 25 |
| 26 | 4 | 3 | 3 | 1 | 4 | 1 | 1 | 3 | 20 |
| 28 | 1 | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 17 |
| 30 | 3 | 2 | 4 | 3 | 2 | 2 | 1 | 3 | 20 |

CG- Control group; EG- Experimental group; 1- Nothing; 2-A bit; 3-Moderate; 4-A lot.

# **Appendix M:** Table of post-exam STAI responses

| Group | ID | I feel exhausted | I feel at ease | At the moment I'm worried about the misfortune that might happen | I'm rested | I feel nervous | I am relaxed | I feel happy | I feel stable | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| CG | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 2 | 4 | 22 |
| | 5 | 1 | 4 | 2 | 2 | 1 | 4 | 3 | 3 | 20 |
| | 7 | 3 | 2 | 3 | 1 | 3 | 2 | 2 | 3 | 20 |
| | 9 | 1 | 2 | 3 | 3 | 2 | 3 | 3 | 3 | 22 |
| | 11 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 2 | 14 |
| | 13 | 3 | 2 | 2 | 3 | 3 | 3 | 2 | 3 | 21 |
| | 15 | 1 | 2 | 3 | 2 | 3 | 2 | 1 | 3 | 17 |
| | 17 | 1 | 4 | 2 | 3 | 1 | 4 | 1 | 1 | 17 |
| | 19 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 32 |
| | 21 | 2 | 3 | 2 | 3 | 3 | 2 | 3 | 3 | 21 |
| | 23 | 1 | 4 | 3 | 4 | 1 | 4 | 3 | 4 | 24 |
| | 25 | 1 | 1 | 4 | 2 | 1 | 3 | 1 | 3 | 14 |
| | 27 | 1 | 4 | 4 | 3 | 1 | 3 | 3 | 3 | 22 |
| | 29 | 4 | 4 | 4 | 3 | 3 | 3 | 2 | 3 | 26 |
| EG | 2 | 1 | 4 | 3 | 4 | 1 | 4 | 3 | 4 | 24 |
| | 4 | 1 | 4 | 1 | 4 | 1 | 4 | 4 | 4 | 23 |
| | 6 | 1 | 4 | 4 | 4 | 1 | 4 | 4 | 3 | 25 |
| | 8 | 1 | 3 | 3 | 2 | 2 | 3 | 3 | 3 | 20 |
| | 10 | 1 | 4 | 3 | 4 | 1 | 1 | 1 | 4 | 17 |
| | 12 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 9 |
| | 14 | 3 | 3 | 3 | 1 | 2 | 3 | 1 | 2 | 18 |
| | 16 | 4 | 3 | 2 | 3 | 3 | 3 | 2 | 2 | 22 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 18 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| 20 | 4 | 2 | 4 | 2 | 2 | 2 | 4 | 1 | 21 |
| 22 | 1 | 2 | 2 | 3 | 2 | 2 | 3 | 3 | 18 |
| 24 | 2 | 3 | 3 | 3 | 3 | 3 | 1 | 3 | 21 |
| 26 | 2 | 3 | 3 | 1 | 2 | 3 | 1 | 3 | 18 |
| 28 | 2 | 3 | 4 | 1 | 2 | 3 | 3 | 3 | 21 |
| 30 | 3 | 3 | 4 | 3 | 4 | 3 | 1 | 3 | 24 |

CG- Control group; EG- Experimental group; 1- Nothing; 2-A bit; 3-Moderate; 4-A lot.

# **Appendix N:** Table of post-exam questionnaire responses

| Group | ID | Understand information given about BS | Anxiety before during or after the exam | If yes which phase | Was the music played during the exam helpful in reducing anxiety | Did we make you listen to the right music to reduce anxiety | If not, why |
|---|---|---|---|---|---|---|---|
| CG | 1 | Yes | No | N/A | N/A | N/A | N/A |
| | 3 | Yes | No | N/A | N/A | N/A | N/A |
| | 5 | Yes | No | N/A | N/A | N/A | N/A |
| | 7 | Yes | Yes | During | N/A | N/A | N/A |
| | 9 | Yes | Yes | During | N/A | N/A | N/A |
| | 11 | Yes | Yes | | N/A | N/A | N/A |
| | 13 | Yes | Yes | Before | N/A | N/A | N/A |
| | 15 | Yes | Yes | During | N/A | N/A | N/A |
| | 17 | Yes | No | N/A | N/A | N/A | N/A |
| | 19 | Yes | No | N/A | N/A | N/A | N/A |
| | 21 | Yes | No | N/A | N/A | N/A | N/A |
| | 23 | Yes | No | N/A | N/A | N/A | N/A |
| | 25 | Yes | Yes | During | N/A | N/A | N/A |
| | 27 | Yes | Yes | Before | N/A | N/A | N/A |
| | 29 | Yes | No | N/A | N/A | N/A | N/A |
| EG | 2 | Yes | No | N/A | N/A | Yes | N/A |
| | 4 | Yes | No | N/A | N/A | Yes | N/A |
| | 6 | Yes | No | N/A | N/A | Yes | N/A |
| | 8 | Yes | No | N/A | N/A | Yes | N/A |
| | 10 | Yes | No | N/A | N/A | Yes | N/A |
| | 12 | Yes | No | N/A | N/A | Yes | N/A |
| | 14 | Yes | Yes | Before, During, and After | Yes | Yes | N/A |

| | | | | | | |
|---|---|---|---|---|---|---|
| 16 | Yes | No | N/A | N/A | Yes | N/A |
| 18 | Yes | No | N/A | N/A | N/A | N/A |
| 20 | Yes | Yes | Before, During, and After | Yes | Yes | N/A |
| 22 | Yes | Yes | During | Yes | Yes | N/A |
| 24 | Yes | Yes | During | No | No | The pain in my leg prevented me from relaxing to the music |
| 26 | Yes | Yes | Before | Yes | Yes | N/A |
| 28 | Yes | No | N/A | N/A | Yes | N/A |
| 30 | Yes | Yes | Before | Yes | Yes | N/A |

CG- Control group; EG- Experimental group; N/A- Not Applicable.