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"Muscoloskeletal Tumors and Tumorlike Lesions: a Wearable Sensor Based Functional Assessment"

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Abstract

This doctoral research project investigated the potential of wearable sensor technologies to objectively evaluate motor function in patients with bone and soft-tissue tumors, with the aim of integrating such assessments into clinical practice. The overarching goal was to develop a sensor-based, wearable evaluation protocol capable of capturing motor performance in ecological, real-world conditions. The project began with a comprehensive literature review, which highlighted the limitations of current assessment approaches, including reliance on laboratory-based motion capture systems, a primary focus on straight-line gait analysis, and the lack of holistic evaluations encompassing postural control, daily-life activity, and preoperative motor function. Only a few studies incorporated wearable sensors, and the literature revealed persistent gaps regarding functional outcomes beyond simple gait metrics. To address these gaps, a methodological study adapted conventional evaluation protocols for the constraints of clinical environments, demonstrating that the Two-Minute Walk Test (2MWT) requires specific straight-line distances to yield valid results. Subsequently, preoperative assessments of patients with bone and soft-tissue tumors revealed that motor impairments can occur prior to surgery, with bone tumors affecting gait abilities more than soft-tissue tumors. Tumor size, however, appeared unrelated to these deficits, emphasizing the importance of evaluating complex motor tasks which may reveal neuromuscular involvements and compensatory strategies. Postoperative assessments further indicated that preexisting levels of physical activity influence recovery trajectories. Active patients demonstrated faster functional recovery and a return to preoperative conditions within six months, whereas sedentary patients exhibited altered gait patterns, reduced muscle strength, and greater postural instability. Finally, a pilot study focused on patients undergoing proximal tibial replacement proposed a holistic evaluation model integrating functional performance, patient-reported outcomes, and objective lifestyle measures. Despite similar gait patterns, variability was observed in perceived functional abilities, psychosocial impact, and activity levels, underscoring the need for subgroup-specific evaluations and tailored rehabilitation protocols. Collectively, the present research demonstrates that wearable sensor-based assessments offer a feasible, objective, and clinically meaningful approach to evaluating motor function across the cancer care continuum. This work represents a foundational step toward clinical translation; future protocol standardization and workflow integration are required for clinical adoption. The findings provide a framework for personalized rehabilitation, prehabilitation, and long-term monitoring in patients with rare and heterogeneous tumor populations.

Chapter 1 – Introduction

1.1 Introduction to Pathology

1.1.1 Tumorigenesis

The terms "tumor" (from the Latin *tumor*, derived from *tumere*, “to swell”) and its synonym "neoplasia" (from the Greek *neo* and *plasia*, “new formation”) are used in medicine to describe a cellular alteration that causes the loss of cellular functionality and leads to uncontrolled growth, culminating in the formation of an abnormal cellular mass (“Definition of tumor - NCI Dictionary of Cancer Terms - NCI”).
Tumor formation represents a dysfunctional aspect resulting from an alteration in the harmony and balance of the elements constituting our body, that is, a change in so-called homeostasis. Tumor cells, possessing unlimited replicative potential, begin to proliferate chaotically and appear no longer sensitive to any regulatory mechanism, neither local (contact inhibition of proliferation) nor systemic. This “revolution” at the DNA level, depending on the damaged genetic segment, leads to cellular replication that transforms the cell into a completely different one.

As thoroughly described in a recent review by Zhang et al. (2024), tumorigenesis is widely understood to be a multistep or multi-stage process. The process of tumor formation begins with an oncogenic mutation in a single somatic cell. Depending on the affected genetic region, this initial mutation can trigger abnormal cell proliferation, gradually transforming the cell into a distinct, abnormal phenotype. As these cells replicate, they accumulate further genetic and epigenetic changes, ultimately giving rise to an irreversible, heterogeneous, and invasive lesion. Although somatic mutations and clonal expansions are common in normal tissues, the development of cancer remains rare, indicating that mutations alone are not sufficient for tumor formation. Additional events, such as environmental risk factors and epigenetic modifications, are necessary to drive early clonal expansion and malignant progression. The subsequent evolution of these clones results from interactions between intrinsic cellular properties and extrinsic factors from the surrounding microenvironment. These external pressures can either limit uncontrolled growth or allow specific transformed clones, cells that have acquired key genetic and epigenetic changes, to develop into tumors.

Over time, these transformed cells continue to accumulate alterations, becoming increasingly malignant, while their microenvironment shifts from tumor-suppressive to tumor-promoting.

As the onset of a tumor generally requires multiple mutational events, tumor development is typically a slow and gradual process extending over several years and accelerates as the tumor mass increases (AIRC, n.d.). During this latency period, the tumor may become detectable through instrumental or clinical means as a consequence of specific symptomatology. This observation explains why, in many cases, tumor diagnosis occurs at an advanced biological stage.

1.1.2 Diagnosis

Early diagnostic assessment aims to identify tumors at an initial stage, before they become clinically detectable, and is crucial for reducing disease-related mortality. The diagnostic process for cancer begins with a comprehensive evaluation of the patient's medical and family history, followed by a thorough physical examination aimed at detecting potential abnormalities (NCIe, 2023). Subsequent investigations typically include a combination of laboratory and imaging tests to determine whether a suspicious lesion may represent malignancy. Laboratory analyses can involve blood chemistry tests, complete blood counts (CBC), cytogenetic studies, tumor marker assays, and increasingly, liquid biopsy, a minimally invasive technique that detects circulating tumor cells or tumor-derived DNA in blood samples (NCIe, 2023). However, abnormal laboratory results alone are insufficient to confirm a cancer diagnosis. Imaging modalities such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US), nuclear medicine scans, bone scans, and positron emission tomography (PET) are routinely used to visualize the internal structures of the body, evaluate suspicious masses, and assess the potential spread of disease (NCIe, 2023). Despite these advances, histopathological confirmation remains the gold standard for diagnosis. A biopsy, performed via needle aspiration, endoscopic retrieval, or surgical excision, allows for microscopic examination of tissue samples by a pathologist, who determines whether cells are benign or malignant and characterizes key histological features such as tumor grade, morphology, and proliferative activity (NCIe, 2023). Following histological confirmation, additional tests are conducted to establish the tumor stage, indicating the extent of disease spread, and to identify molecular and genetic markers relevant for prognosis and treatment planning. This integrated, multi-modal diagnostic

approach forms the foundation of precision oncology, ensuring accurate disease characterization and guiding personalized therapeutic strategies (NCIe, 2023).

1.1.3 Classification

The mass that develops within the organ of origin is referred to as the *primary tumor*. Tumors are classified as either benign or malignant, based on fundamental differences in invasiveness and capacity for spread. *Benign tumors* are generally of lesser clinical concern unless they grow to a size that interferes with the normal function of the affected organ or produce excessive amounts of biologically active substances, such as hormones. In contrast, *malignant tumors* have the capacity to spread through the circulatory or lymphatic systems, infiltrate adjacent tissues and to generate metastases, colonizing distant organs, thereby disrupting and eventually replacing their normal (NCIb, n.d.). Cells in malignant tumors are typically less differentiated than normal cells, and their characteristics may change over time. Nevertheless, they retain certain features of their tissue of origin, allowing classification according to their resemblance to the corresponding normal tissue. From a developmental standpoint, all cells originate from three embryonic germ layers: the endoderm, mesoderm, and ectoderm. Based on this classification, malignant tumors are termed carcinomas when derived from endodermal or ectodermal tissues, and *sarcomas* when arising from mesodermal tissues.

Tumor cells may detach from the primary tumor and, through the lymphatic and/or hematogenous circulation, disseminate to virtually any organ in the body, giving rise to *metastases* (also known as secondary lesions). The confinement of a normal cell within a specific organ or tissue is maintained by both physical barriers and complex interactions that occur between cells. The basement membrane, located beneath the epithelial cell layers and the endothelial lining of blood vessels, represents the most important physical barrier separating different tissues. Metastatic cells, however, are able to overcome this barrier by degrading the components that constitute the basement membrane (NCIc, 2025). The duration of the process of migration to distant sites in the body, where they establish new colonies, varies greatly among individuals and depends on the specific type of cancer (Cooper, 2000). Metastases represent the most advanced stage of the disease and are responsible for approximately 90% of all cancer-related deaths.

Cancer staging refers to the extent of disease at diagnosis, including the size of the primary tumor, the involvement of nearby lymph nodes, and whether there is distant metastasis (NCIa, 2022). The stage of a cancer plays a pivotal role in assessing prognosis, selecting appropriate therapeutic strategies, and identifying eligibility for clinical trials. To determine the stage, physicians may order imaging studies, laboratory tests, and other diagnostic procedures (NCIa, 2022). The most widely used system is the TNM classification (Tumour-Node-Metastasis), in which "T" describes the size and local spread of the primary tumor, "N" denotes the number and extent of regional lymph-node involvement, and "M" indicates the presence (M1) or absence (M0) of distant metastases. These letters are followed by numerical values (for example, T2 N1 M0) that provide further granularity. Many tumors are subsequently grouped into broader stages, such as Stage 0 (in situ), Stage I/II/III (varying degrees of local/regional spread), and Stage IV (distant metastasis), which simplify classification for treatment decision-making and registry purposes (NCIa, 2022). Although staging describes the disease at diagnosis, it remains fixed even if the cancer later advances or recurs, and changes in tumor status are captured in additional documentation rather than a revision of the original stage (NCIa, 2022).

Tumor grade describes how closely cancer cells resemble their normal counterparts when examined under a microscope, and it is a critical factor in guiding treatment planning and estimating prognosis. Specifically, well-differentiated (low-grade) tumors feature cells that still resemble normal tissue, tend to grow and spread more slowly, and are often less aggressive. In contrast, poorly differentiated or undifferentiated (high-grade) tumors have cells that appear very abnormal, typically exhibit rapid growth and dissemination, and generally require more intensive therapeutic interventions (NCIf, 2022). While tumor stage reflects the size and spread of the cancer, grade is distinct and focuses on cellular biology rather than extent of disease. Most grading systems use a numerical or alphabetical scale, such as Grade X (undetermined), 1 (low), 2 (intermediate), 3 (high), and 4 (undifferentiated), with higher numbers indicating greater deviation from normal morphology (NCIf, 2022). The grade is typically determined by a specialist pathologist following evaluation of a tumor sample obtained via biopsy; this pathology report integrates cellular appearance, differentiation status and other histological features (NCIf, 2022). Given its prognostic and therapeutic significance, tumor grade is routinely used in conjunction with other factors – including stage, genetic characteristics of the tumor, and the patient's overall health status – to formulate an individualized treatment plan. In practice, a high-grade tumor may prompt

more aggressive initial treatment to mitigate the risk of rapid progression or metastasis (NCIf, 2022).

1.1.4 Clinical Treatment

The primary objective of cancer therapy is to eliminate tumor cell proliferation and to prevent both potential local recurrence and distant metastases. This goal is achieved through a combination of surgical, radiotherapeutic, and pharmacological treatments, alongside the integration of novel therapeutic techniques developed in recent decades. The choice of the most appropriate treatment depends on the tumor's specific characteristics, including histology, anatomical location, and potential systemic spread.

Surgery remains one of the main treatment modalities, particularly for tumors diagnosed at an early stage. In benign tumors, complete *excision* of the mass offers a high likelihood of definitive cure. In malignant tumors, surgery typically involves not only tumor removal but also excision of surrounding tissues and nearby lymph-nodes to reduce the risk of recurrence. Oncologic microsurgery and the use of laser techniques are often employed to minimize the risk of metastatic spread and to operate on particularly delicate tissues.

Radiotherapy, initially limited to a few tumor types, has seen significant advancements through the development of technologies that allow precise targeting of deep tumors while minimizing damage to healthy tissues. Advanced techniques, such as intraoperative radiotherapy and hadron therapy, further enhance treatment efficacy.

On the pharmacological front, *chemotherapy* remains an essential component, often used in combination with other treatments according to specific dosing regimens. New therapeutic modalities, such as photodynamic therapy, utilize photosensitizing agents activated by lasers to selectively target tumor cells. Hormonal therapy and immunotherapy provide additional approaches for treating specific tumors, such as hormone-dependent cancers, through the use of hormones, anti-hormones, and monoclonal antibodies. In certain immunotherapeutic procedures, repeated inoculation of ethanol into the neoplastic mass via a long needle under ultrasound guidance (percutaneous alcoholization) aims to enhance the limited capacity of the immune system to control tumor growth.

Finally, *pain management* represents a crucial aspect of oncology care, addressing one of the most severe symptoms experienced by cancer patients. Pain may manifest early in some tumors and predominantly in advanced stages in others. The World Health Organization

(WHO) has developed specific guidelines for managing cancer-related pain. In addition to pharmacological therapy, invasive and semi-invasive techniques are employed to deliver analgesics, both local and opioid, to the spinal roots (epidural analgesia) or to the central nervous system (subarachnoid spinal or intraventricular techniques), modulating the transmission of pain signals (spinal neuromodulation) and thereby improving the quality of life of patients affected by cancer.

1.1.5 Bone and Soft Tissue Tumors

As previously stated, tumors might be benign or malignant. A malignant tumor that arises from bone or from the body's soft tissues, encompassing cartilage, adipose tissue, muscle, vascular tissue, and other connective or supportive structure is called sarcoma (Cirstoiu et al., 2019).

Benign bone tumors are more common nevertheless malignant tumors have greater clinical significance due to their invasive nature and metastatic potential. Common benign bone tumors include osteochondroma, osteoma, osteoblastoma, chondroma, giant cell tumor, ossifying fibroma, and fibrous dysplasia, are often asymptomatic and discovered incidentally. These lesions are often asymptomatic and incidentally discovered. When present, symptoms may include bone pain, swelling, deformity, functional limitation, pathological fractures, or compression of adjacent structures. Treatment depends on tumor type, size, location, and symptoms. Observation is appropriate for small, asymptomatic lesions, whereas symptomatic or high-risk tumors may require surgical excision, sometimes supplemented by pharmacological therapies such as bisphosphonates for giant cell tumors. Radiotherapy is rarely indicated, reserved only for cases where surgery is not feasible.

Malignant bone tumors are characterized by aggressive growth and potential metastasis, most frequently to the lungs. Primary malignant bone tumors include osteosarcoma, Ewing sarcoma, chondrosarcoma, chordoma, and giant cell tumor with malignant transformation. Osteosarcoma primarily affects adolescents and young adults, often in the metaphyses of long bones. In Italy, bone sarcomas have an annual incidence of just over 1 case per 100,000 individuals (AIRC, 2025). Diagnosis requires integration of radiologic and histopathologic findings, with imaging modalities including X-ray, CT, and MRI, confirmed by biopsy. Treatment involves multimodal therapy combining surgery with neoadjuvant and adjuvant

chemotherapy. Advances in limb-sparing surgery have reduced amputation rates to less than 10%, and pulmonary metastasectomy is critical in cases of oligometastatic disease.
Ewing sarcoma, predominantly affecting children and young adults, is highly chemosensitive and radiosensitive. Multimodal therapy is standard, with prognosis largely dependent on tumor response to induction chemotherapy. Chondrosarcoma, more common in adults, is primarily treated surgically, with chemotherapy reserved for dedifferentiated or mesenchymal subtypes. Chordomas, slow-growing tumors of the axial skeleton, are treated mainly with surgery, and in selected cases, particle therapy due to the difficulty of achieving wide surgical margins.

Soft Tissue Tumors originate from non-epithelial tissues, excluding bone and hematolymphoid neoplasms. They range from benign lesions to aggressive sarcomas. Soft tissue tumors are rare, with an incidence of approximately 5 cases/100,000 (Sbaraglia et al., 2021). Etiological factors include trauma, prior radiation exposure, chemical agents, and genetic syndromes (e.g., Li-Fraumeni, neurofibromatosis type I, Gardner syndrome). Classification is based on tissue differentiation: myofibroblastic, fibroblastic, adipocytic, smooth and striated muscle, vascular, neural, chondro-osseous tumors, and tumors of uncertain differentiation.
Soft tissue sarcomas (STSs) account for about two-thirds of all sarcoma cases. They most commonly arise in the extremities or superficial trunk, but can also involve the head, neck, internal organs (including the uterus), or deep trunk regions, particularly the retroperitoneum, a posterior portion of the abdominal cavity rich in adipose and connective tissue (AIRC, 2021).
Although rare, STSs are more frequent than bone sarcomas, they can affect various tissues, including muscle, adipose tissue, and blood vessels. The global incidence is slightly higher in men than in women and exhibits a bimodal age distribution, with peaks between 10–20 years and 60–70 years. In Italy, STSs affect approximately 5 individuals per 100,000 per year, representing about 1% of all malignant tumors (AIRC, 2021).
Diagnosis of STTs requires a multidisciplinary approach integrating clinical assessment, imaging (MRI, CT, PET), histopathology, immunohistochemistry, and molecular analysis. Treatment is primarily surgical, aiming for wide excision margins. Radiotherapy is recommended for high-risk or incompletely resected tumors, while chemotherapy is reserved for high-grade sarcomas, metastatic disease, or chemosensitive tumors such as

rhabdomyosarcoma. Targeted therapies, including tyrosine kinase inhibitors for Ewing sarcoma, are emerging based on molecular profiling.

The most common *symptoms* associated with sarcomas of the lower limbs include:
Mass or swelling: sarcomas often present as a painless lump in the leg or foot. Over time, the mass may enlarge and become painful, particularly if it compresses nearby nerves or muscles;
Pain: although many sarcomas do not initially cause pain, as they grow, they may exert pressure on nerves, leading to discomfort or pain, especially during movement;
Difficulty in movement: when the tumor develops near a joint, it may restrict mobility, making it difficult to bend or extend the leg;
Systemic symptoms: in some cases, more general symptoms such as fever or weight loss may occur, particularly in advanced stages of the disease.
Throughout life, it is common to experience several of the symptoms mentioned above, many of which are transient and associated with non-pathological conditions. However, in some instances, such symptoms may represent the earliest warning signs of a tumor. When a symptom persists over time or increases in intensity, it is essential not to ignore it and to consult a physician for further evaluation. Early diagnosis is crucial in oncology, as a thorough understanding of symptoms, together with awareness of their potential seriousness, can have a significant and positive impact on disease progression and therapeutic outcomes.

1.1.6 Orthopedic Oncological Treatments, Functional Abilities and Quality of Life

Sarcomas arise mainly in joints and limbs (lower limbs 46% and upper limbs 18%) and the primary aim of oncological surgery is the complete tumor removal to optimize survival and minimize recurrence. Over the years, advances in surgical techniques have led to a progressive replacement of amputations with limb salvage procedures. Depending on the tumor type, location, size, tumors are treated through limb-salvage surgical resections or excisions. Whenever the patient's condition permits, and depending on the extent of the tumor, surgical management may include marginal excisions, wide excisions, and resection, usually followed by reconstruction of the affected area. Several reconstructive techniques can be employed, with the selection influenced by factors such as tumor location, size,

histological type, and patient-related considerations including age, lifestyle, and local tissue status. Therefore, it is the biological and anatomical characteristics of the tumor that primarily determine the surgical approach, rather than the anticipated functional outcomes that may follow.

In particular, the main reconstructive options for bone tumors include segmental bone transport, resection arthrodesis, bone graft reconstruction, and modular endoprosthetic reconstruction. (Cirstoiu et al., 2019), and, for soft tissue tumors, local excision, wide excision, and compartmental resection. In more advanced cases of both bone and soft tissue tumors, a radical excision, meaning amputation of the affected limb, may be required. It is evident that the heterogeneity of sarcomas, and tumors in general, results in a wide range of surgical approaches, each highly individualized and tailored to the specific case, contributing to the overall heterogeneity among sarcoma patients. However, the present thesis will not focus primarily on the diverse range of orthopedic surgical approaches, but rather on the post-surgical outcomes and the impact they may have on the patient's functional abilities and quality of life, while also describing the clinical heterogeneity of the patient population.

The term functional ability refers to an individual’s capacity to perform everyday activities and tasks that are ordinarily expected in daily life. The concept of quality of life refers to an assessment of the overall well-being of individuals and communities, encompassing the extent to which a person is able to realize life’s opportunities and derive satisfaction from daily living.

The benefits of the limb salvage approach are well established, aiming to enhance patient satisfaction by facilitating early mobility, stability and weight-bearing, thereby promoting better recovery, improved quality of life, cosmetic appearance, and emotional acceptance. However, the resection of large segments of bone or soft tissue often results in varying degrees of physical impairment and disability. Moreover, complex reconstructive procedures and the large size of the implants (megaprostheses) are associated with both immediate and delayed implant-related complications, including mechanical failure, aseptic loosening, infection, dislocation, and neurovascular injury.

Postoperative symptoms and limitations commonly reported by patients include stiffness (60%), weakness (51%), fatigue (33%), pain (31%), limited range of movement (29%), and swelling (10%). In the lower extremity, most studies indicate that limb-salvage surgery provides superior functional outcomes compared with amputation, as amputees generally exhibit poorer overall function (Ruggieri et al., 2011). A study by Weschenfelder et al. (2020) identified several factors that critically influence post-therapeutic outcomes following

musculoskeletal sarcoma operations. Patients who necessitated amputation reported significantly poorer function and quality of life across multiple dimensions (including mobility, daily activities, and physical functioning) compared to those receiving limb-preserving operations. Regarding anatomical location, sarcomas affecting the lower extremity resulted in descriptions of poorer mobility and greater "Anxious Preoccupation," indicating that this patient subgroup requires greater support for both postoperative rehabilitation and occupational reintegration. Conversely, neither the size of the tumor (classified by TNM staging) nor the administration of adjuvant radiotherapy was found to significantly impact post-therapeutic function, quality of life, or coping strategies. Crucially, the achieved post-therapeutic function demonstrated a direct linear relationship with postoperative quality of life, as well as several domains of mental coping.

1.1.7 Pre- and Post-Operative Patients Assessment

In the majority of studies, particularly those conducted in the past, the systems predominantly employed for the evaluation of patient condition, encompassing both psychosocial dimensions and functional capabilities, are based on various questionnaire models. These are summarized by a recent review by Ramsey et al. (2020) as follows.

For disease specific measures:
Patient-Reported Outcomes (PROs) which consist of evaluations of a patient's health status obtained directly from the patient, elucidating their subjective experience without clinician interpretation.
Toronto Extremity Salvage Score (TESS), a disease-specific PRO used for functional outcomes in bone and soft tissue sarcomas of the upper and lower extremity. It is considered as highly reliable, valid, and widely used, soliciting information on the difficulty of various activities of daily living (ADLs) (Davis et al., 1996).
Musculoskeletal Tumor Rating Scale (MSTS), a disease-specific measure covering six areas (pain, function, emotional acceptance, general functional ability, gait handicap, and use of gait aides), scored on a 0-5 Likert scale (Enneking et al., 1993).

For general health measures and Computer Adaptive Testing (CAT):

36-Item Short Form Health Survey (SF-36) is a proprietary PRO instrument widely reported in sarcoma research that measures general health across eight categories, typically partitioned into physical and mental components.
Patient-Reported Outcomes Measurement Information System (PROMIS), developed by the National Institutes of Health, is a non-proprietary general health measure across multiple domains of mental, physical, and social well-being. It employs Computer Adaptive Test (CAT) methods to generate the most informative subsequent question, resulting in shorter questionnaires compared to instruments like the TESS.

For Health State Utility Measures (HSUs):
HSUs are PROs that incorporate a patient's self-evaluation of their health state and the population's preference for that state. They are normalized to a single numeric value (usually between 0 and 1) and are crucial for comparative effectiveness research and economic analysis (cost-utility analyses).
EuroQol-5D (EQ-5D): A widely used HSU instrument that evaluates HRQL in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (EuroQol Group, 1990).
Short Form-6D (SF-6D): An HSU instrument based on the SF-36, which transforms SF-36 data into utility scores suitable for economic analysis (Mukuria et al., 2025)7.

For objective functional assessment:
Gait and ambulatory ability can be assessed by measuring parameters such as velocity, stride, strength, and energy efficiency, often estimated by oxygen consumption.
The Physiological Cost Index (PCI) is a lab method measuring energy efficiency using only walking heart rate, resting heart rate, and distance walked (Hagberg et al., 2011).

For real world activity monitoring:
Wearable Activity Monitors consist of instruments such as the Step Watch Activity Monitor, which measure acceleration to track free-living activity and estimate activity intensity. Accelerometers have shown promise in providing objective functional assessment in sarcoma patients and conveying information not contained in standard HRQL scores.

The prevalence of questionnaires in research can be attributed to their ease of use and cost-effectiveness, which renders them a more favorable option in comparison to alternative

objective measurement methods. Patient-reported outcomes (PROs) are designed to capture the subjective experience of patients. However, even physician-based assessments, such as the Musculoskeletal Tumor Society (MSTS) score, are affected by provider reporting bias, with studies demonstrating statistically significant discrepancies in which clinicians tend to rate functional outcomes higher than patients themselves (Ramsey and Gundle, 2020).

It is important to acknowledge that these measures are inherently subjective and are influenced by the patient's own perception. Furthermore, while these tools provide valuable information regarding the ability of a patient to perform specific movements, and if so, the level of pain experienced, they offer limited insight into the quality of movement, that is, not only whether a patient is able to perform a movement, but rather the various ways in which it is performed. This can only be accurately described through objective parameters assessing the manner of execution.

Additionally, objective measures of physical activity have a modest correlation with PRO and HRQL scores (Jelsma et al., 2021). This finding suggests that patient reported surveys may not fully capture critical aspects of functional performance in daily activities. These aspects can be more effectively assessed through real-world activity tracking methods (Smith and Guerra, 2021).

Concurrently, the prevailing objective assessment methodologies, encompassing laboratory-based analyses, comprising metabolic testing and comprehensive gait analysis, are characterized by their invasiveness and expense, necessitating the utilization of bulky equipment and the establishment of sophisticated laboratory environments. This characteristic renders them impractical for widespread use in treatment centers. Moreover, there is frequently an absence of real-world correlation: observations in controlled laboratory environments do not necessarily mirror variations in real-world physical activity or functional capability (Fowler et al., 2021).

1.2 General Objectives of the Thesis

Despite the extensive reliance placed in previous research on patient-reported outcomes and laboratory-based assessments aimed to evaluate functional recovery, both approaches are inherently limited in their capacity to provide a comprehensive and accurate assessment of the subject's recovery. Subjective measures are affected by perception bias, while laboratory analyses, despite their accuracy, lack ecological authenticity and are impractical for clinical routine use. To date, there remains a lack of objective, non-invasive, and ecologically valid

quantification of movement capable of evaluating the quality of movement in real-world contexts.

Addressing this gap necessitates the integration of wearable sensors, which can provide continuous, quantitative, and contextually relevant measures of movement. This methodological approach facilitates a more comprehensive evaluation of motor function, thereby addressing the current gap between subjective reports and controlled laboratory analyses.

The present study aims to understand the use of wearable sensors for objective evaluation in tumor patients and their application in the clinical setting. The aim of the present PhD study is to develop a wearable, sensor-based evaluation protocol and to objectively assess motor function in tumor patients in real-world, ecological conditions. This wearable-based evaluation protocol will allow to explore the characteristics of this heterogeneous population through an accurate and reliable evaluation of movement in ecological contexts, providing objective data that complement traditional clinical assessments.

1.3 Thesis Structure

The thesis chapters are organized to address the main objectives of this study progressively, moving from the theoretical foundations to the empirical investigation and the practical application in clinical settings. This structured approach follows patients from the initial stages of their orthopedic treatment journey to their reintegration into normal living, offering a comprehensive and systematic exploration of the subject matter.

Chapter 1: introduction

The present chapter furnishes the clinical and scientific background by introducing limb-salvage surgery for bone and soft tissue sarcomas. It defined the research problem, objectives and hypotheses, emphasizing the importance of evaluating functional outcomes and quality of life in oncological orthopedic patients.

Chapter 2: literature review and selection of assessment tools

A comprehensive review of the literature on functional outcomes following limb-salvage surgery is presented. Current knowledge is summarized and gaps in the literature are identified. The rationale for selecting the most appropriate functional assessment instruments is also explained.

Chapter 3: Methodological study on clinical test

This chapter focuses on a methodological study about the adaptation of the 2MWT, a key functional mobility test, to clinical constraints. The study investigates the test's feasibility when performed in different path lenghts, exploring potential adaptations to accurately evaluate patient functional capacity.

Chapter 4: Tumor characteristics and impact on functional outcomes

This chapter examines how tumor-related variables, such as type and size, affect functional outcomes. Comparative analyses are conducted between patients with bone and soft tissue sarcomas to explore how these factors influence preoperative functional performance.

Chapter 5: Physical activity and postoperative recovery

This chapter analyses the relationship between preoperative physical activity and postoperative recovery. It investigates whether higher baseline activity levels contribute to faster or more effective rehabilitation and highlights the role of physical activity as a predictive factor for better functional outcomes.

Chapter 6: Pilot study and long-term functional evaluation

This chapter presents the findings of a pilot study conducted on patients approximately one year or more after surgery. The aim of the study was to identify key parameters for a comprehensive long-term evaluation using a biopsychosocial assessment model. Attention is given to evaluating patients in real-world settings, beyond the limitations of clinical testing.

Chapter 7: General discussion and conclusions

This chapter integrates and critically discusses findings from previous chapters, situating the results within the broader context of oncologic orthopedics and patients' care. The chapter also addresses methodological considerations, limitations and implications for clinical practice and future studies.

This final chapter summarizes the thesis's key outcomes, highlighting their scientific and clinical significance, and proposes directions for future research and applications in clinical practice.

Chapter 2 – Literature Review

The present chapter provides a thorough review of existing literature on functional outcomes and assessment methods for patients undergoing limb-salvage surgery for bone and soft tissue tumors. The primary aim is to synthesize current knowledge, highlight methodological approaches, and identify gaps that justify the present research. Emphasis is placed on the selection and application of functional assessment tools, which are essential for accurately evaluating postoperative recovery and quality of life. This review lays the groundwork for the methodological study and empirical analyses presented in subsequent chapters.

2.1 Search Strategy

A literature search was conducted using PubMed database with a predefined query focused on functional outcomes in patients undergoing limb-salvage surgery for bone and soft tissue sarcomas emphasizing motion analysis and the characteristics of this patient population in terms of locomotion and functional abilities. The literature search employed the following terms: *(bone tumor OR bone neoplasms OR sarcoma) AND (gait analysis OR IMU OR wearable sensors)*. Only articles published in English were considered. Studies were included if they reported objective functional assessments, either alone or in combination with patient-reported outcome measures. Articles reporting solely on questionnaire-based assessments, with no objective functional measurement, were excluded. The literature search was conducted up to and including December 2022. Only articles published by this date were considered, resulting in a total of 29 articles selected for full-text review and inclusion in the study.

2.2 Results: Functional Outcomes in Sarcoma Patients

To provide a comprehensive overview of the reviewed literature, a summary framework was developed to categorize the key characteristics of the included studies. This framework highlights three main aspects: the types of reconstructive surgery employed; the objective measurement tools used to assess functional outcomes; and the subjective assessment instruments reported. The resulting schematic representation is presented in Table 1.

Table 1 *– Objective functional assessments: instrumentation, tasks and parameters assessed*

Author	Aim	Surgical Intervention	Instrumentation	Task	Parameters Measured
Kim et al. 2021	Analysis of the kinetic and kinematic characteristics based on tumor location in patients with endoprosthetic knee replacements following bone tumor resection	LSS - Endoprosthetic knee replacement	Motion capture system (8 cameras), force plates	Linear walk (7m)	Spatiotemporal parameters, joint angles, joint moments, joint power, GRF
Singh et al. 2018	To assess gait patterns as an objective measure of functional outcomes in patients undergoing knee tumor resection and endoprosthetic reconstruction	LSS - Endoprosthesis reconstruction of the knee	Motion capture system (6 cameras)	Linear walk (15m), self-selected speed	Spatiotemporal parameters, knee joint angle
Carmody et al. 2012	To evaluate gait parameters and functional outcomes in patients after periacetabular resection with ischiofemoral pseudoarthrodesis or soft tissue reconstruction	LSS - Periacetabular resection, pseudoartrodesis or no bone reconstruction	Motion capture system (12 cameras)	Linear walk (non-specified)	Spatiotemporal parameters
Bruns et al. 2016	To determine how distal femur megaprosthesis implantation affects gait patterns	LSS - Distal femoral resection, megaprosthesis	Motion capture system, force plates	Linear walk (25m)	Spatiotemporal parameters, joint angles, GRF, muscle activation
Okita et al. 2013	Not declared - case report	LSS - distal femur resection, endoprosthesis	Motion capture system (7 cameras), force plates	Linear walk (6m), self-selected speed	Spatiotemporal parameters, joint angles, joint moments, joint power, GRF; knee strength
Hillmann et al. 2000	To evaluate muscle activity, kinetics, and kinematics after rotationplasty and their association with functional outcomes	Rotationplasty	Motion capture system (4 cameras), force plates, EMG	Linear walk (12m)	Joint angles, joint moments, muscle activation
Benedetti et al. 2013	To test whether the APC implant improves hip control during gait in both sagittal and coronal planes through biological muscle reconstruction	LSS - Proximal femur bone resection, modular prosthetic replacement or allograft-prosthesis composite	Motion capture system, EMG	Linear walk (10m)	Spatiotemporal parameters, kinetic, kinematic, muscle activation
Benedetti et al. 2000	To assess locomotor function in relation to quadriceps muscle resection and residual strength in patients treated for distal femur malignant bone tumors	LSS - Distal femur resection, endoprosthesis	Motion capture system, force plates, EMG, dynamometer	Linear walk, self-selected speed; voluntary maximum contraction	Spatiotemporal parameters, muscle strength, muscle activation
Catani et al. 1993	To evaluate functional performance using gait analysis of kinetic, kinematic, and temporal-distance parameters	The Van Nes rotationplasty	Motion capture system, force plates	Linear walk (15m), self-selected speed	Spatiotemporal parameters, joint angles, GRF
Bozkurt et al. 2005	To examine dynamic effects of proximal, middle, and distal fibulectomy through detailed gait analysis	LSS - Proximal fibula resection vs. distal fibula resection	Motion capture system	Linear walk (10m), self-selected speed	Spatiotemporal parameters, joint angles, joint moments, muscle activation
Mo et al. 2019	To investigate bone injury characteristics in endoprosthetic knee replacement patients during walking using musculoskeletal dynamics and finite element analysis	LSS - Distal femur resection, endoprosthesis	Musculoskeletal finite element model (OpenSim)	Linear walk	Joint moments
Wingrave & Jarvis 2018	To describe gait parameters, energy expenditure, and joint kinematics in an internal hemipelvectomy patient after chondrosarcoma excision and rehabilitation (case study)	LSS - Pelvic resection and acetabulum resection	Motion capture system, forceplates	6MWT	Spatiotemporal parameters, joint kinematics, 6MWT total distance
Carty et al. 2009	To evaluate kinematic and kinetic features after limb salvage and identify predictors of gait dysfunction, including surgery timing, muscle/bone resection, knee strength/ROM, and prosthetic type.	LSS - Bone resection, endoprosthesis and expandable prostheses	Motion capture system (8 cameras), forceplates	Linear walk (6.4m), self-selected speed	Joint angles, joint moments, joint power, GRF
Furtado et al. 2019	To assess the feasibility, acceptability, and validity (face, discriminant, convergent, concurrent) of accelerometer-based body-worn monitors for balance, gait, and TUG	LSS and amputation	Stopwatch, video step count, wearable accelerometers	7-meter TUG test; 120s standing (balance);	Balance: RMS, jerk, f95 Gait spatiotemporal parameters

				intermittent fast walk (7m)	
Furtado et al. 2016 (review)	To systematically review studies measuring balance, gait, and physical activity in lower extremity sarcoma patients using clinically translatable methods	-	Forceplates, foot switches, gaitmat, StepWatch activity monitor, pedometer	-	-
Kask et al. 2019 (review)	To identify methods used to measure functional outcomes in patients surgically treated for lower-extremity soft tissue sarcoma	-	-	-	-
Ramsey & Gundle 2020 (review)	To provide an overview of functional assessment methods	-	-	-	-
Filiset al. 2022 (review)	To review prosthetic reconstructions after lower limb tumor resection, evaluate gait outcomes versus healthy individuals, and estimate changes in gait parameters to inform pre-surgical planning	-	-	-	-
Alexander et al. 2021	To review patient-reported and objective gait outcomes in pediatric patients with proximal tibial defects after osteosarcoma resection and combined prosthetic-biologic reconstruction.	LSS - Proximal tibial resection, prosthetic biologic reconstruction (pediatric)	Motion capture system	Linear walk (10m), self-selected speed	The Gait Profile Score (GPS)
Okita et al. 2014	To examine kinematic and kinetic changes during fast walking in patients after endoprosthetic knee replacement and guide strategies for increasing walking speed	LSS - Bone resection, endoprosthetic knee replacement	Motion capture system (7 cameras), forceplates	Linear walk (6m), self-selected speed and faster speed	Spatiotemporal parameters, joint angles, GRF
Pesenti et al. 2018	To compare knee function via gait analysis after megaprosthesis versus allograft reconstruction in distal femur limb salvage patients	LSS - Bone resection, Reconstruction with either 1) megaprosthesis or 2) allograft augmented with fibular graft	Motion capture system (6 cameras), forceplates	Linear walk (9m), self-selected speed	Spatiotemporal parameters, joint angles, GRF
De Visser et al. 2000	To quantify compensatory changes in temporal gait parameters, muscle activity, and knee kinematics during treadmill walking in patients with LSS of the knee or hip	LSS - knee surgery and hip surgery	Footswitches, electrogoniometers, EMG	Gait laboratory assessment. Task details not specified	Spatiotemporal parameters, joint angles, muscle activation
Basteck et al. 2022	To examine the impact of an 8-week individualized exercise program on gait function in adolescents and young adults with lower extremity megaendoprostheses	LSS - Bone resection, distal femur or proximal tibia replacement	Motion capture system (8 cameras)	Linear walk (15m), self-selected speed; TUG; TUDS	Joint angles
Rompen et al. 2000	To assess gait patterns as an objective outcome in femur tumor patients after endoprosthetic reconstruction and compare them with subjective functional measures	LSS - Femur resection, endoprosthetic reconstruction	Footswitches, electrogoniometers	Linear walk (7m), self-selected speed	Spatiotemporal parameters, joint angles
AlGheshyan et al. 2015	To compare gait mechanics of distal femur allograft versus metallic endoprosthetic reconstruction relative to healthy controls	LSS - Bone resection, distal femur endoprosthesic recontruction or allograft reconstruction	Motion capture system (8 cameras), forceplates	Linear walk, self-selected speed	Spatiotemporal parameters, joint angles, CoP for balance
Tsuboyama et al. 1994	To evaluate gait after limb-salvage surgery using pedography and examine its correlation with knee extension strength	LSS - Distal femur resection, modular uncemented prosthesis	Plantar pressure measurement system, dynamometer	Linear walk (10m), own, self-selected slow walking pace; maximal volountary contraction	Joint angles, joint moments, muscle strength
Jaegers et al. 1995	To determine kinematic parameters and motion patterns of the trunk, hip, and knee in transfemoral amputees	Transfemoral amputee	GIGA-system (K-lab), electrogoniometers	Linear walk (7m), self-selected speed, fast walking speed	Spatiotemporal parameters, joint angles

Kawai et al. 2000	To assess gait abnormalities and functional impairment in patients after prosthetic reconstruction following tumor resection	LSS - Proximal femur resection and reconstruction (intraarticular resection of the hup), total hip replacement or bipolar iplant	Footswitches, indirect calorimetry system	Free walking (not specified)	Spatiotemporal parameters, energy cost
Visser et al. 2003	To assess the extent of functional recovery in patients after limb-sparing surgery	LSS - Distalfemoral knee prosthesis,proximal femoral hip prosthesis, saddle prosthesis	Treadmill, foot switches	Linear walk, self-selected speed, dual task	Spatiotemporal parameters

2.2.1 The Reconstructive Interventions

The reconstructive interventions employed across the reviewed studies primarily focus on limb-salvage surgery (LSS) techniques following the resection of musculoskeletal tumors, predominantly around the knee and hip joints (Furtado et al., 2017; Ramsey and Gundle, 2020). These procedures aim to preserve joint function while addressing extensive bone and soft tissue defects (Singh et al., 2018).

The primary types of reconstructive interventions observed in the literature include:

Endoprosthetic Replacement (Modular and Megaprostheses)

The reviewed studies predominantly focus on reconstructive interventions, such as limb-salvage surgery, following resection of musculoskeletal tumors around the knee and hip joints (Furtado et al., 2017; Furtado et al., 2020; Ramsey and Gundle, 2020). These procedures aim to preserve joint function while addressing extensive bone and soft tissue defects (Singh et al., 2018).

Endoprosthetic reconstruction is the basis of modern surgical management following resection of an extremity bone tumor (Ramsey and Gundle, 2020). Modular endoprostheses are the most commonly used, especially for knee tumors, and they enable preservation of limb function in sarcoma patients (Kim et al., 2021a; Singh et al., 2018).

For distal femur and proximal tibia tumors, modular or megaprosthetic systems are widely used. Examples of these systems include the Modular Universal Tumor and Revision System (MUTARS; Implantcast GmbH), the Howmedica Modular Resection System (HMRS), the Kyocera Limb Salvage System, the JMM K-MAX KNEE System K-5 (Carty et al., 2009; Okita et al., 2014a), and the Stanmore SMILES™ system, which is available in fixed-hinge, rotating-hinge, and expandable configurations (Carty et al., 2009). The Kotz Modular

Femur-Tibia Reconstruction (KMFTR) is an uncemented modular prosthesis that has been studied for distal femoral resections (Tsuboyama et al., 1994).

For proximal femur reconstruction, modular prosthetic replacement is a frequently adopted strategy following tumor excision (Benedetti et al., 2013). Numerous studies have evaluated the functional outcomes and postoperative gait following femoral endoprosthetic reconstruction (Rompen et al., 2002).

MUTARS hemipelvic prostheses and saddle prostheses have been employed for pelvic reconstruction following periacetabular or hemipelvic resections to restore stability and ambulation (Carmody Soni et al., 2012).

Biological and Allograft Reconstructions

Biological reconstruction techniques often involve structural allografts, which are sometimes combined with prosthetic components to create composite constructs. These approaches aim to restore skeletal continuity while facilitating biological integration and muscle reattachment.

Allograft-prosthesis composites are commonly used, especially for proximal femur reconstructions. They allow for the reattachment of residual muscles, such as the abductors and iliopsoas. This improves hip control compared to modular endoprostheses (Benedetti et al., 2013). Allograft-prosthesis composites have also been used following periacetabular tumor resections (Carmody Soni et al., 2012).

Massive allografts remain a frequent choice after wide resections. Outcomes of distal femoral allografts have been compared with those of metallic endoprosthetic replacements (AlGheshyan et al., 2015; Bruns et al., 2016). In some cases, allografts augmented with fibular grafts have enabled epiphysis-sparing reconstructions, and the functional outcomes have been evaluated against those of megaprostheses (Pesenti et al., 2018). Bone allografts have long been essential to limb-salvage approaches for high-grade extremity osteosarcoma. Another technique for periacetabular defects is ischiofemoral pseudoarthrodesis, and depending on defect size and patient factors, no reconstruction is performed in select cases (Carmody Soni et al., 2012).

Specialized Techniques and Soft Tissue Reconstruction

Specialized approaches are essential for soft tissue and extensor mechanism reconstruction, especially in the proximal tibia. After tumor resection, reconstruction of the knee extensor

mechanism is critical. Methods include the patellar-loop technique (Pilge et al., 2015) and pedicled fibular transfer, which is especially important in pediatric osteosarcoma (Alexander et al., 2021).

Adequate soft tissue coverage is also crucial. The medial gastrocnemius flap is commonly used after proximal tibial resection to safeguard the prosthesis and improve local vascularity (Singh et al., 2018). Several studies have confirmed its effectiveness with megaprostheses. Vascularized free fibula flaps provide biological integration and long-term durability for extensive defects. However, donor site morbidity, including pain, ankle instability, and reduced strength, remains a concern (Feuvrier et al., 2016).

Ablative/Functional Techniques

In addition to biological and endoprosthetic approaches, ablative and functional reconstructive techniques are used to manage malignant bone tumors of the lower limbs. These techniques are employed when conventional limb-salvage reconstruction is not feasible or when optimal function can be achieved through biomechanical adaptations.

One well-established procedure is rotationplasty, also known as the Borggreve–Van Nes technique. It involves resecting the tumor-bearing segment and rotating the distal limb 180 degrees, allowing the ankle to function as a new knee joint. Rotationplasty is primarily indicated for tumors of the distal femur or proximal tibia and has demonstrated satisfactory long-term functional and psychological outcomes, particularly in younger patients (Hillmann et al., 2000; Hopyan et al., 2006).

Amputation is a critical option when limb-salvage surgery is contraindicated due to tumor extent, neurovascular involvement, or compromised local tissues. Studies comparing limb-salvage surgery and amputation generally indicate that LSS preserves mobility and independence better than amputation (Furtado et al., 2020; Hillmann et al., 2000; Hopyan et al., 2006). Nevertheless, amputation remains necessary in cases where local control or prosthetic reconstruction cannot ensure adequate function or oncological safety (Aksnes et al., 2008).

2.2.2 Methods of Functional Assessment and Biomechanical Analysis

The following is a list of the methods of functional assessment and biomechanical analysis that were employed in the analyzed literature:

A comprehensive evaluation approach is indicated for assessing functional outcomes following limb salvage procedures for musculoskeletal tumors, particularly in the knee and hip regions. This evaluation strategy employs a multifaceted approach that integrates subjective clinical scores, objective physical assessments, and advanced motion analysis techniques. The objective of these various assessments is to quantify the remaining physical capabilities and analyze compensatory gait strategies.

Clinical and Subjective Outcome Measures

Standardized scoring systems are frequently employed to furnish subjective functional data derived from patient reports or clinician observations.

The Musculoskeletal Tumor Society (MSTS) Score is a measurement developed for functional evaluation of reconstructive procedures. The MSTS score assesses six specific categories for the lower extremity: pain, function, emotional acceptance, use of supports, walking ability, and gait (Enneking et al., 1993). Each category is rated on a scale from 0 to 5 points, resulting in a maximum total score of 30 points. This maximum total score is often expressed as a percentage of the maximum possible score (Enneking et al., 1993; Furtado et al., 2017; Hillmann et al., 2000).

The Toronto Extremity Salvage Score (TESS) is a disease-specific measure focused on assessing physical disability through a self-administered questionnaire that rates the difficulty experienced in performing thirty daily activities. Typically, TESS scores range from 0, representing the worst possible outcome, to 100, representing the best possible outcome (Furtado et al., 2017).

Questionnaires such as the Quality of Life–Cancer Survivors (QoL-CS) and the EORTC QLQ-C30 are utilized to assess overall quality of life, including functional and symptom scores (Basteck et al., 2022; Furtado et al., 2017).

Specialized Functional Scales are also employed in this context. Measures include the Knee Society Score (KSS) and the Functional Mobility Scale (FMS) (Alexander et al., 2021). The modified Ambulation Score (A1/A2) is a measurement that evaluates comfortable and fast walking ability, distance, and ease of walking in various circumstances (Rompen et al., 2002).

Objective Biomechanical Movement Analysis

Gait analysis in the reviewed papers generally employs several three-dimensional motion capture systems (Basteck et al., 2022; Benedetti et al., 2013; Carmody Soni et al., 2012;

Catani et al., 1993; Furtado et al., 2017; Kim et al., 2021a). These systems employ retro-reflective markers strategically positioned on anatomical landmarks in accordance with established protocols, such as the Plug-in Gait protocol (Okita et al., 2014a, 2013; Pesenti et al., 2018) or the Helen Hayes marker set (Carty et al., 2009; Kim et al., 2021a). Data acquisition frequently involves the use of force plates, used to record ground reaction forces (GRFs) during the gait cycle (AlGheshyan et al., 2015; Bruns et al., 2016; Catani et al., 1993; Kim et al., 2021a).

The following list contains the measured parameters from the present studies' gait analysis.

Spatio-Temporal Parameters

These metrics have been employed to quantify the spatial and temporal dimensions of walking, and the task performed is predominantly a linear walk.

Velocity is a significant component in the majority of the analyzed studies, primarily evaluated as preferred walking velocity or, in a limited number of cases, as faster walking speed (Okita et al., 2014a; Rompen et al., 2002; Singh et al., 2018). A significant body of research has revealed that patients often exhibit reduced mean walking velocity compared to healthy controls (Carty et al., 2009; Pesenti et al., 2018; Rompen et al., 2002; Singh et al., 2018; Wingrave and Jarvis, 2019).

Stride length (m) and step length (m) are also common measurements (Catani et al., 1993; Pesenti et al., 2018; Rompen et al., 2002; Singh et al., 2018).

Stance phase duration (% cycle or seconds), swing phase duration, stride time, gait cycle time, cadence (steps/min), and double-limb support time (Bruns et al., 2016; Catani et al., 1993; Furtado et al., 2020; Rompen et al., 2002) are also measured. Patients frequently demonstrate asymmetry, particularly with a reduced stance phase on the affected leg compared to the non-affected leg (Carty et al., 2009; Rompen et al., 2002; Singh et al., 2018).

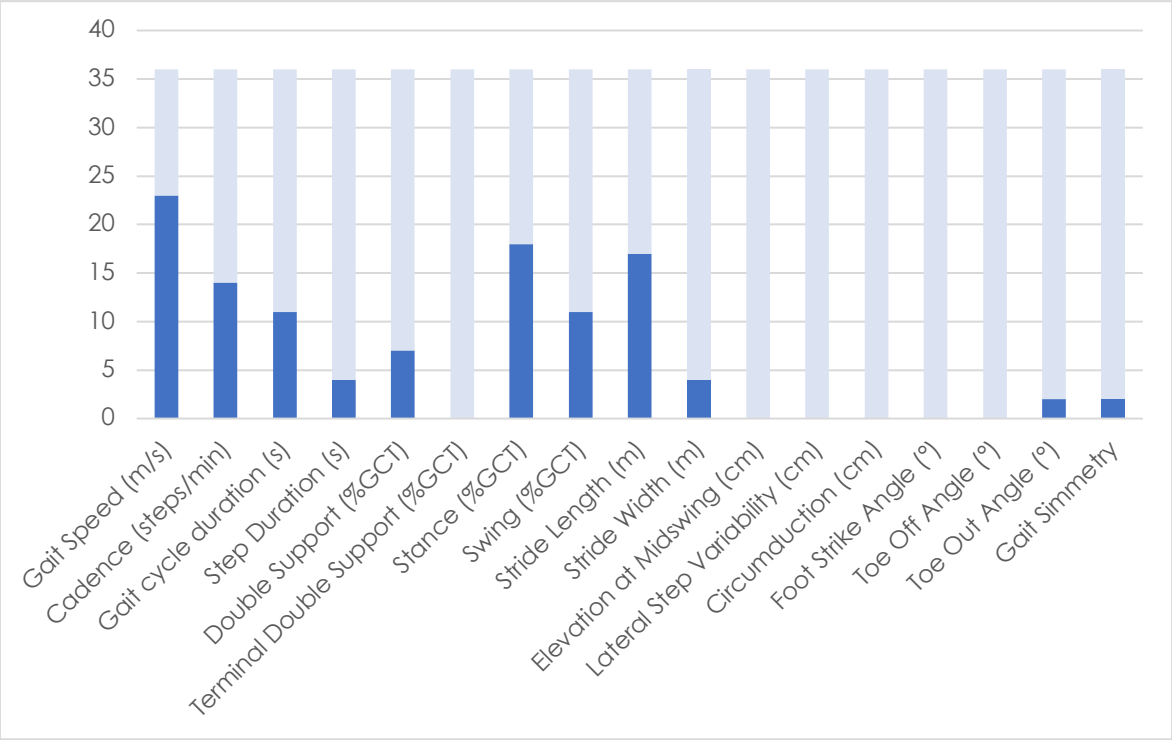

Figure 1 *– Frequency of reported spatiotemporal parameters in the literature: number of studies in which each parameter was used.*

Kinematic Parameters

These metrics are used to describe joint motion and angular displacement in degrees.

A particular focus is placed on knee flexion during loading response, which is frequently diminished, resulting in a condition known as "stiff knee gait" (Benedetti et al., 2013; Bruns et al., 2016; Carty et al., 2009; Rompen et al., 2002). Other observed patterns include hyperextension during stance (de Visser et al., 2003; Pesenti et al., 2018) or "flexed knee gait" (Okita et al., 2013; Rompen et al., 2002). It has been demonstrated that maximal ankle dorsiflexion during stance may be increased, particularly in proximal tibia groups (Kim et al., 2021a). The Gait Deviation Index (GDI) and the Gait Profile Score (GPS), instead, are metrics that integrate complex 3D data into a single score, thereby quantifying overall gait pathology (Basteck et al., 2022; Pesenti et al., 2018).

Kinetic Parameters

These measures are derived from force calculations, which are determined through the implementation of inverse dynamics analysis.

Ground reaction forces (GRFs) (i.e., fore-aft, vertical, mediolateral components) are measured, including maximum loading response and peak vertical GRF (Benedetti et al., 2000; Bruns et al., 2016; Kim et al., 2021a; Okita et al., 2014a, 2013).

Joint moments (net force generated by muscles) and ankle torque are also assessed (AlGheshyan et al., 2015; Benedetti et al., 2000; Carty et al., 2009; Kim et al., 2021a), as well as joint powers (energy generated or absorbed per unit time) (Carty et al., 2009; Kim et al., 2021a).

Electromyography (EMG)

Surface EMG is used to record electrical activity and on-off timing of specific muscles during the gait cycle, including the quadriceps, hamstrings, gastrocnemius, tibialis anterior, and gluteus medius (Benedetti et al., 2000; Bruns et al., 2016; De Visser et al., 2000; Hillmann et al., 2000). In the present studies EMG is used to identify muscle coordination, which may reveal co-contraction in the affected or contralateral limb (Bruns et al., 2016; De Visser et al., 2000).

Body-Worn Monitors

Triaxial accelerometer-based monitors placed on the lower back have been used for objective quantification of functional tasks. The outcomes measured included the area of postural sway (ellipsis, m^2/s^4), the magnitude of sway (RMS, m/s^2), the jerkiness (jerk), and the frequency of sway (f95, Hz) (Furtado et al., 2020). For the gait analysis, instead, outcomes of interest include step time, total gait time, step length, step velocity, and the time taken to complete the 7-meter instrumented Timed Up-and-Go (iTUG) test. The iTUG time has demonstrated strong correlation with the stopwatch TUG time (Furtado et al., 2020).

Physical and Strength Tests

Complementary tests are utilized to assess physical function and muscle strength quantitatively.

The Range of Motion (ROM), generally performed using a handheld goniometer, was assessed with a focus on the active and passive range of motion, particularly knee flexion and extension (Carty et al., 2009; Singh et al., 2018; Tsuboyama et al., 1994).

Isokinetic Strength Testing was used to measure peak extension and flexion torque at specific angular velocities (e.g., 30°/s or 90°/s) using a dynamometer (Benedetti et al., 2000; Okita et al., 2013; Tsuboyama et al., 1994).

Manual Strength Assessment, to assess muscle strength, is typically conducted through the utilization of established protocols, such as the Medical Research Council (MRC) scale (Carty et al., 2009).
Timed Functional Tests such as the 6-Minute Walk Test (6MWT) (Wingrave and Jarvis, 2019), the standard Timed Up-and-Go (TUG) test (Furtado et al., 2025), and the Timed Up and Down Stairs (TUDS) test (Basteck et al., 2022) were used to measure physical capability and endurance.

In summary, the functional status of patients undergoing limb salvage is characterized through a combination of subjective reports (MSTS, TESS), objective quantification of movement (Gait Analysis parameters including kinetics, kinematics, and EMG), and targeted physical measures (isokinetic strength, ROM). This comprehensive approach is capable of fully capturing the extent of impairment, as well as functional compensation. However, it appears that a clear evaluation protocol has not yet been established.

2.2.3 Gait and Functional Outcomes Following Limb Salvage

The objective functional assessment measures employed across the studies yielded several quantifiable results concerning gait mechanics, kinematic deviations, kinetic function, and stability following limb salvage procedures for lower extremity sarcomas.
Gait analysis studies consistently demonstrate altered biomechanical patterns in patients following surgical intervention using endoprosthetic replacement or biological reconstruction for bone tumors around the knee and hip (Bruns et al., 2016; Furtado et al., 2020; Rompen et al., 2002; Singh et al., 2018). While limb salvage generally yields favorable subjective functional scores, such as the Musculoskeletal Tumor Society (MSTS) score, instrumental gait assessment reveals specific deficits (Enneking et al., 1993; Singh et al., 2018).

General Gait Performance and Spatiotemporal Outcomes

A comprehensive review of the present literature reveals that patients who underwent limb-salvage surgery exhibited reduced walking efficiency and asymmetrical gait characteristics compared to healthy controls. These impairments are indicative of both mechanical and neuromuscular adaptations that occur following extensive reconstructive procedures.

Patients exhibited a substantial decrease in gait speed compared to healthy subjects, generally ranging from 68% to 88% of normal walking speed (Rompen et al., 2002; Singh et al., 2018). A meta-analytic examination of the existing literature reveals that prosthetic reconstructions resulted in a mean reduction in gait velocity of −0.17 m/s compared to non-implanted subjects (Filis et al., 2022). In individual studies, mean self-selected walking speeds were reported at approximately 0.91 m/s in patients with wide resection and endoprosthesis replacement around the knee, approximately 68% of the normative value of 1.33 m/s (Singh et al., 2018). Such reductions in velocity are indicative of compromised propulsion and compensatory gait strategies, often resulting from muscle weakness or reduced joint range of motion. Correlated parameters include reduced cadence, shorter stride length, and a shortened stance phase duration for the operated limb, reflecting reduced time of load bearing on the involved leg (Bruns et al., 2016; Rompen et al., 2002; Singh et al., 2018; Tsuboyama et al., 1994). In patients with prosthetic reconstructions, on average, stride length (normalized to height) was reduced by 6.95%, while cadence decreased by 4.65 steps per minute relative to healthy counterparts (Filis et al., 2022). These findings underscore the global reduction in gait rhythm and efficiency that is typically observed in sarcoma patients following extensive limb reconstruction.

Decreased peak vertical ground reaction forces during heel-strike and toe-off, suggests a cautious gait pattern aimed at minimizing stress on the reconstructed knee (Bruns et al., 2016; Tsuboyama et al., 1994). Despite decreased parameters compared to norms, some studies report a symmetrical gait pattern between the affected and unaffected limbs, implying compensation by the contralateral side (Singh et al., 2018).

Although some studies have reported a symmetrical gait pattern between the affected and unaffected limbs, suggesting compensatory adaptation by the contralateral side and preservation of the inter limb symmetry in parameters such as stride length, gait velocity, and knee range of motion (Singh et al., 2018), the majority of research findings has documented substantial asymmetrical adaptations in post-surgical gait. For instance, patients with femoral endoprostheses frequently exhibited a prolonged swing phase and reduced stance duration on the operated limb compared with the contralateral side (Rompen et al., 2002). Conversely, the uninvolved limb exhibited a compensatory increase in stance phase duration to maintain balance and forward propulsion (De Visser et al., 2000; Rompen et al., 2002).

Kinematic Results (Joint Movement Patterns)

Abnormal joint kinematics, particularly involving the knee, were consistently observed among patients with endoprosthetic reconstructions, indicating significant deviations from normal physiological gait patterns.

Patients frequently exhibited reduced knee flexion during the loading response phase on the (Carty et al., 2009). Kinematic analysis frequently identifies a "stiff-knee" gait pattern in the operated limb compared to both the contralateral limb and healthy controls. This is characterized by reduced knee flexion during the loading response phase (the initial flexion occurring immediately after heel strike) (Benedetti et al., 2000; Carty et al., 2009; Pesenti et al., 2018). This stiff-legged gait is generally linked to quadriceps weakness or dysfunction resulting from necessary muscle resection, prompting patients to maintain a more extended knee position during stance for stability (Benedetti et al., 2000; Pesenti et al., 2018). Alternatively, some patients exhibit a "flexed knee gait" with reduced knee extension during the latter half of the stance phase (Okita et al., 2013; Rompen et al., 2002). This pattern is associated with decreased propulsive capacity at push-off, correlating with slower walking speeds and shorter contralateral step lengths (Okita et al., 2013).

Altered motion patterns at the hip and ankle joints frequently accompanied these knee abnormalities, suggesting a chain of compensatory mechanisms across the lower limb. In a particular study, 9 out of 18 patients who underwent endoprosthetic reconstruction demonstrated irregular hip flexion–extension profiles during ambulation (Rompen et al., 2002). Patients who underwent proximal tibia resections exhibited a tendency to maintain a persistently flexed hip throughout the gait cycle when compared to patients with distal femoral graft (Rompen et al., 2002). This observation likely reflects a compensatory postural adaptation.

Kinetic Results (Forces and Moments)

Kinetic analysis was employed to elucidate the functional impairments associated with endoprosthetic reconstruction. This analysis entailed the quantification of the altered distribution of forces and joint moments during gait. These findings establish a direct link between surgical reconstruction characteristics and biomechanical performance.

Distinct alterations in ground reaction force profiles were observed in the operated limb. Specifically, the vertical GRF was reduced during the loading response and terminal stance

phases, indicating diminished weight acceptance and push-off capability. Conversely, an increased GRF during mid-stance suggested compensatory overloading in this phase (Carty et al., 2009). Furthermore, the maximal anterior shear force during terminal stance, indicative of forward propulsion, was also reduced in the reconstructed limb, thereby emphasizing the limited propulsive power (Carty et al., 2009).

According to Carty et al. (2009), among the factors that influence postoperative function, the extent of soft tissue resection is the most significant predictor, with knee extension strength ranking second. These findings underscore the pivotal role of preserved musculature and extensor mechanism integrity in restoring functional gait mechanics after limb-salvage procedures.

Altered joint moment patterns were also evident, reflecting compensatory neuromuscular adaptations. In patients demonstrating a flexed knee gait, the maximal ankle plantarflexion internal moment was significantly lower on the operated side compared to both the contralateral limb and healthy controls (Okita et al., 2013). This reduction indicates a potential decrease in the effectiveness of the push-off mechanism, which may be attributable to weakened calf musculature or altered mechanical leverage following reconstruction.

Overall, the kinetic evidence indicates a global redistribution of forces across the lower limb, characterized by reduced propulsive efficiency and reliance on compensatory loading strategies, which are directly associated with the degree of surgical soft tissue compromise.

Intervention comparisons

Research comparing tumor location has identified differential gait patterns. In patients who underwent distal femoral replacement, as indicated by the findings of Kim et al. (2021a), a propensity for knee extension was observed. Instead, patients who underwent proximal tibial replacement exhibited an increase in maximal dorsiflexion during stance, with the hip remaining in a flexed position throughout the gait cycle. Furthermore, maximal knee flexor moment during midstance was found to be significantly higher in the proximal tibial replacement patients compared to both controls and the distal femoral replacement grup (Kim et al., 2021a).

The integrity and function of residual musculature are crucial determinants of functional outcome. The amount of soft tissue removal is identified as a primary predictive factor of postoperative disability, overshadowing the influence of time from surgery or resected bone

length (Carty et al., 2009). Patients frequently employ compensatory mechanisms involving the ipsilateral ankle and contralateral hip joints (Okita et al., 2013).

A comparison of megaprosthesis and allograft reconstruction techniques for distal femur tumors reveals that both megaprosthesis and epiphysis-sparing allograft groups exhibited generally acceptable long-term functional outcomes and minimal gait impairment. The available literature reveals no significant differences between the two techniques with respect to gait parameters or overall functional indices, such as the Gait Deviation Index (AlGheshyan et al., 2015; Pesenti et al., 2018). However, megaprosthesis patients exhibited a more pronounced decrease in knee flexion throughout the stance phase compared to allograft patients, resulting in an extension moment applied to the prosthesis hinge (Pesenti et al., 2018).

In the context of proximal femoral reconstruction, studies have been conducted that compare modular prosthetic replacement to allograft-prosthesis composite. These studies have shown that patients undergoing modular prosthetic replacement exhibited reduced walking speeds and distinct hip extension pattern at toe-off, suggesting compromised iliopsoas function (Benedetti et al., 2013). To compensate for this deficit, patients displayed altered neuromuscular strategies, including increased hip abduction and greater activation of the homolateral erector spinae, likely compensating for loss of iliopsoas function due to soft-tissue detachment. These findings underscore the mechanical and neuromuscular adaptations imperative to maintain gait stability following proximal femoral reconstruction (Benedetti et al., 2013).

Allograft-prosthesis composite implants, designed for biological reinsertion of residual abductors and iliopsoas tendons onto the allograft, hypothesize better functional hip control, although differences in subjective outcome scores may not always be substantial (Benedetti et al., 2013; Kawai et al., 2000).

Comprehensively, prosthetic technology facilitates functional gait restoration. However, kinematic deviations and compensatory strategies persist as reconstruction-specific concerns, necessitating customized rehabilitation to ensure optimal biomechanical recovery.

Gait analysis following Van Nes rotationplasty (VNR) has been shown to confirm that the procedure provides a functionally viable reconstruction (Catani et al., 1993; Hillmann et al., 2000). Although the patient's gait exhibited temporal-distance abnormalities, such as reduced velocity and stride length, the movement was characterized as smooth and

coordinated due to active control of the converted ankle joint ("pseudo-knee") (Catani et al., 1993). Patients with VNR demonstrated reduced propulsive phase forces on the prosthetic side (Catani et al., 1993). The functional outcome scores obtained in this study are comparable to those reported for prosthetic knee replacement (Hillmann et al., 2000). Additionally, a younger age at the time of surgery was found to be significantly correlated with superior postoperative gait performance (Hillmann et al., 2000).

A longitudinal evaluation of patients who underwent vascularized free fibula flap revealed quantifiable donor site morbidity affecting gait (Feuvrier et al., 2016). Patients exhibited reduced walking speed, decreased cadence, and shorter stride length compared to the control group (Feuvrier et al., 2015). Notably, the donor leg demonstrated increased variability during ambulation, indicating a subconscious adoption of a "cautious approach" to mitigate the risk of falling (Feuvrier et al., 2016).

Objective Balance and Activity Measures

The integration of wearable inertial sensors into postoperative assessment provided valuable quantitative insight into balance, stability, and functional activity, complementing traditional gait laboratory analyses and clinical scales.

Patients who underwent limb-salvage reconstructions exhibited substantial balance impairments when compared to healthy controls. Objective sway parameters derived from accelerometer data indicated impaired postural control:

Ellipsis (sway area) — a significant elevation is observed in patients, indicative of a greater displacement of the center of mass.

Root mean square (RMS) values are indicative of the magnitude of sway and reduced static stability, with elevated values corresponding to greater sway and diminished static stability.

Jerk: Elevated jerk values have been shown to indicate a reduction in the smoothness of sway and a compromise in fine motor control during quiet standing (Furtado et al., 2020).

These findings collectively pointed toward decreased postural stability and increased neuromuscular effort to maintain upright balance following reconstruction.

The application of advanced technologies, such as accelerometer-based body-worn monitors, is supported as a feasible and objective tool for quantifying balance and gait disturbances in lower extremity sarcoma patients, showing good validity against clinical scales (Furtado et al., 2020). Preliminary evidence suggests that dedicated exercise interventions may induce positive effects on gait indices and functional outcomes (TESS, MSTS) in survivors with endoprostheses, advocating for the potential benefit of regular,

tailored rehabilitation programs (Basteck et al., 2022). Also, a case study by Wingrave & Jarvis (2019), demonstrated that after a personalized intensive rehabilitation training, the gait pattern of a patient who underwent a wide excision of a chondrosarcoma had improved, becoming similar to the control group, highlighting the importance of specific post-operation treatments.

The relationship between clinical scores and other variables is a subject that merits further investigation. Objective movement data exhibited moderate yet statistically significant correlations with subjective functional scales, thereby reinforcing the clinical relevance of sensor-derived measures. Walking velocity exhibited a moderate positive correlation with the overall MSTS score, as well as with its function and walking sub-scores. These findings indicate that faster, more efficient gait is associated with higher perceived function (Singh et al., 2018; Wingrave and Jarvis, 2019). Sway area exhibited a moderate negative correlation with MSTS, indicating that greater postural sway corresponded to poorer self-reported function (Furtado et al., 2020).

Overall, these findings underscore the augmented diagnostic value of wearable technologies in discerning subtle impairments in stability and performance that may not be adequately captured by conventional clinical or observational assessments. This, in turn, has the potential to enhance postoperative monitoring and individualized rehabilitation planning.

2.3 Discussion

Overall, literature provides information about the differences, in terms of gait spatial-temporal parameters, limb kinematics, and muscle activity, among several prosthetics' implantations (e.g., allograft vs modular prosthetics implants after proximal femur resection etc.) (Benedetti et al., 2013; Kim et al., 2021a; Pesenti et al., 2018), or the effects of the level of the resection and the removal of specific muscles (Benedetti et al., 2000; Bozkurt et al., 2005). Instead, Carty et al., (2009), demonstrated the amount of soft tissue removal to be a predictive factor of gait dysfunction.

A recent review by Filis et al., (2022), makes the point of gait deviations after prosthetic reconstruction in patients with lower limb resection. They revealed that patients generally exhibit a reduction of spatiotemporal parameters such as gait velocity, stride length, and cadence, and display a longer cycle time. However, it seems that specific training can reduce gait dysfunctions (Basteck et al., 2022; Wingrave and Jarvis, 2019). In addition, a review by Furtado et al. (2017), revealed that sarcomas patients exhibited worse gait and balance

performance, and physical activity levels compared to healthy controls, both in the short and long term. However, in almost all the analyzed studies, evaluation protocols are limited to straight walking tasks, eventually performed at different speeds (Jaegers et al., 1995; Okita et al., 2014a).

Applicability and Integration into Clinical Practice

It should also be noticed that, in clinical practice, clinicians and medical doctors make large use of qualitative questionnaires and scales based on patients' or clinicians' subjective evaluations, rather than relying on objective performance outcomes (Kask et al. 2019). Validated questionnaires such as the Musculoskeletal Tumor Society Scoring System (MSTS) or the Toronto Extremity Salvage Score (TESS) are usually administered by the clinicians themselves to obtain information about the disability level, joint impairments and stability, muscle strength, but also emotional acceptance, etc. (Furtado et al., 2017). Results are reported as a scale of values, but do not provide any objective measurement of the motor performance, crucial for determining the success of the surgical intervention and the efficacy of the rehabilitative treatment. An objective measurement such as the gait analysis may provide clinicians with information on the limbs' kinetic and kinematic parameters, offering an in-depth description of possible gait deviations and compensation strategies that impacts daily life activities and patient quality of life and, consequently, determines the goodness or failure of the surgical intervention.

Recent literature also highlighted how the instruments used in most of the analyzed studies lack consistency, validity, and reliability specific to sarcomas patients (Furtado et al., 2017). Stereophotogrammetric systems remain the gold standard for kinematic assessments, but other smaller, portable, and cost-effective devices, such as footswitches, and pedometers, are widely used. However, Ramsey et al. (2020) underline that in most of the studies, these devices do not properly collect significant functional information, while accelerometers could provide a more accurate estimation of patient's activity. Although the gold standard laboratory-based motion capture and force platforms offer precise biomechanical insights, they require specialized facilities and trained personnel, which limits their routine clinical applicability. In contrast, wearable inertial measurement units (IMUs) and accelerometry-based devices provide portable, ecologically valid, and scalable alternatives that can be easily integrated into clinical and home-based assessments. These systems enable the

continuous monitoring of gait, balance, and activity, which facilitates individualized rehabilitation and long-term outcome tracking (Furtado et al., 2017; Iosa et al., 2016).

2.4 Wearable sensors for functional assessment: principles, applications, limitations

Wearable technology, also known as "wearables," is defined as miniaturized electronic devices that are characterized by their ease of donning and doffing, as well as their integration into clothing and accessories (Smuck et al., 2021). These devices are fundamentally changing biomedicine by enabling continuous, longitudinal health monitoring outside of traditional clinical settings (Dunn et al., 2018). Quantitative functional assessment, such as gait analysis, is crucial for evaluating human movement patterns to identify markers of pathology, injury, or other characteristics (Benson et al., 2018).

Historically, the gold standard for advanced gait analysis involved the use of costly 3D motion capture and force plate equipment, necessitating the expertise of trained personnel and demanding extensive time for data collection and analysis (Benson et al., 2018). This methodological approach imposes limitations on accessibility and frequently fails to capture the nuances of an individual's movement patterns in a real-world, daily-life context (Benson et al., 2018). In contrast, wearable devices offer significant advantages due to their portability, affordability, and broad applicability across various populations, including healthy individuals, older adults, and those with chronic illnesses (Benson et al., 2018).

Principles of Wearable Sensing

Wearable devices employed for health applications can be broadly classified into three categories: mechanical, physiological, and biochemical sensor types (Dunn et al., 2018). For the purpose of functional assessment, mechanical sensors, particularly those that utilize Inertial Measurement Units (IMUs), are most common (Dunn et al., 2018).

Typically, an IMU consists of three mutually orthogonal gyroscopes and three orthogonal accelerometers, and occasionally, a 3-axis magnetometer (Iosa et al., 2016; Kobsar et al., 2020). Accelerometers are designed to measure linear acceleration, while gyroscopes are engineered to detect angular velocity (Kobsar et al., 2020). The term "inertial" is derived from the principle that these sensors measure their own movement by exploiting the

reluctance of a contained mass to move when acted upon by external forces or torques (Iosa et al., 2016).

Segment Orientation and Sensor Fusion

The primary challenge in employing IMUs for kinematic analysis lies in the estimation of the orientation of the body segment to which the sensor is attached (Picerno, 2017). Segment orientation is typically determined by numerical integration of the measured angular velocity. However, this process is susceptible to time-increasing errors known as drift (Picerno, 2017).

In order to mitigate drift and improve orientation estimates, sensor fusion algorithms are employed, combining data from multiple sensors.

1. Accelerometers are used to determine orientation relative to gravity, particularly to correct errors in the roll and pitch angles of a sensor or body segment (Picerno, 2017).
2. Magnetometers are capable of detecting the local magnetic North, thereby providing an absolute reference that can be used to correct drift in the vertical direction, otherwise known as the yaw angle. This capability enables a full three-dimensional (3D) orientation estimate (Iosa et al., 2016; Picerno, 2017).

Placement and Setup

The anatomical placement of a wearable device should be selected based on the specific research question. For instance, the analysis of whole-body running patterns related to stiffness or impact might utilize placement on the lower back (Benson et al., 2018). Conversely, the investigation of foot strike patterns necessitates the placement of sensors on the foot (Benson et al., 2018). In the context of daily life walking analysis, placement near the center of mass, such as the waist or lower back, has been identified as the most common location (Benson et al., 2018).

A critical prerequisite for estimating functionally meaningful 3D joint kinematics is the alignment of the sensor-to-segment axis, which is often achieved through calibration procedures that relate the sensor's embedded reference system to the anatomical axes of the body segment (Picerno, 2017).

Applications in Functional Assessment

Wearable IMUs are broadly applied across six main areas of clinical human movement analysis, including gait analysis, stabilometry (static balance), instrumented clinical tests,

upper body mobility assessment, daily-life activity monitoring, and tremor assessment (Iosa et al., 2016).

Gait and Locomotion Analysis

Wearables are extensively used for quantitative gait analysis, encompassing both walking and running patterns (Benson et al., 2018). These sensors facilitate the calculation of fundamental spatiotemporal parameters, such as velocity, step time, and stride length (Benson et al., 2018). It is important to note that inertial measurement units (IMUs) also facilitate the extraction of advanced metrics, providing insights into the quality, not just quantity, of gait (Benson et al., 2018). The key outcomes of this study include variability, regularity, symmetry, and dynamic stability (Benson et al., 2018).

The validity of inertial measurement units (IMUs) has been demonstrated to be excellent for the assessment of mean spatiotemporal parameters, including step time, stride time, and length during walking, in healthy adults (Kobsar et al., 2020).

While the aggregation of data from multiple sources is often challenging due to the heterogeneity inherent in study designs, inertial measurement units (IMUs) have emerged as a valuable tool for the measurement of lower limb joint angles, particularly in the sagittal plane. In this regard, IMUs have demonstrated a high degree of validity and reliability, with reported values ranging from good to excellent (Kobsar et al., 2020).

The monitoring of pathological populations (e.g. Parkinson’s Disease) is a crucial aspect of medical research and practice. Wearable devices offer a highly objective, accurate, and continuous monitoring of movement disorders, thereby overcoming the limitations associated with the subjectivity and inconsistency of traditional clinical assessment scales and patient self-reporting (Del Din et al., 2016; Lu et al., 2020).

For example, wearable sensors, typically gyroscopes or accelerometers, exhibit high specificity (88%) and sensitivity (95%) in quantifying motion retardation associated with bradykinesia (Del Din et al., 2016). Wearables facilitate objective instrumentation of clinical assessments, such as the Timed Up and Go (TUG), enabling the segmentation of mobility subcomponents, including turning duration and time-to-sit (Lu et al., 2020).

Moreover, accelerometers are utilized to quantify the frequency and amplitude of pathological tremors, which typically occur at frequencies above 4 Hz in Parkinson's disease (Lu et al., 2020).

Wearable sensors have been developed to continuously monitor gait characteristics (rhythm, symmetry, stride length). These sensors can provide insights into the prognosis of gait disorders. Devices capable of detecting freezing of gait (FOG) and falls with a high degree of accuracy have been developed. In some cases, the accuracy of these devices has been reported to exceed 90% (Lu et al., 2020).

Daily-Life Activity Monitoring

The potential for data collection without the constraints of a laboratory setting represents a significant benefit of wearable inertial measurement units (IMUs). This capacity facilitates long-term, unrestricted monitoring of human movement in real-life conditions (Iosa et al., 2016). In the field of research, inertial measurement units (IMUs) have been utilized as actigraphs, which are instruments designed to quantify the volume and classify the type of activities performed by subjects. These activities can include sedentary behaviors, such as sitting or lying, as well as dynamic events that are crucial for assessing autonomy and lifestyle (Iosa et al., 2016).

Limitations and Challenges

Despite their transformative potential, the adoption and reliability of wearable sensors in clinical practice face several significant technical, methodological, and implementation challenges.

The calculation of kinematic variables, which are not directly measured but rather derived through integration (such as joint kinematics), is inherently susceptible to errors (Iosa et al., 2016).

Sensor fusion techniques rely on magnetometers to correct for yaw drift; however, these sensors are sensitive to ferromagnetic disturbances, which are common in clinical environments and can negatively affect the reliability of the estimated 3D orientation (Iosa et al., 2016; Picerno, 2017).

Moreover, while mean spatiotemporal parameters demonstrate high accuracy, the reliability and validity of advanced measures, specifically spatiotemporal variability and symmetry metrics, are frequently found to be poor to moderate (Kobsar et al., 2020). These discrepancies are presumably attributable to an absence of optimized and standardized protocols (e.g., variability in the number of steps or processing techniques) (Kobsar et al., 2020).

Another significant challenge lies in the lack of high-quality studies and comprehensive statistical reporting within this domain. A significant number of studies are constrained by underpowered or unjustified sample sizes (Kobsar et al., 2020). Subsequent research endeavors must entail meticulous designs and incorporation of both relative (e.g., ICC) and absolute (e.g., Limits of Agreement, Standard Error of Measurement) statistical metrics to guarantee robustness (Kobsar et al., 2020).

Practical barriers to widespread adoption include ensuring that devices are not too bulky, remembering to charge devices, and dealing with varying levels of acceptance and potential stigma associated with wearing the technology (Dunn et al., 2018). Moreover, the financial burden associated with high device costs, in conjunction with the necessity for compatible infrastructure (e.g., smartphones and wireless access), might impede accessibility, particularly among patients in low-resource settings (Dunn et al., 2018; Smuck et al., 2021). However, wearable sensors offer significant advantages over traditional in-lab analysis, including the ability to more fully understand real-world movement patterns.

2.5 Gap: need for ecological studies and objective data on patients with musculoskeletal tumors

As pointed out by Iosa et al., (2016), nowadays, wearable inertial sensors are a valid measurement tool, sufficiently accurate, less bulky, and more user-friendly than other complex measurement systems. They are widely used to instrument clinical tests and daily activities, as they are able to suitably assess spatiotemporal gait parameters, allowing patients to perform activities of daily living without the restrictions imposed by the laboratory environment, thus providing a more ecological assessment. Furthermore, a study by Furtado et al. (2020), provided information on the feasibility and validity of body-worn monitor assessment of gait and balance in patients treated for lower extremity sarcomas, demonstrating the ability of body-worn accelerometers of distinguishing between patients and control group functional outcomes.

Also, the review of the extant literature reveals that all studies included in the analysis assessed patients at least one year following surgical intervention, thereby reflecting long-term functional outcomes. However, a notable limitation is the absence of objective preoperative evaluations, as well as longitudinal data capturing the trajectory of functional recovery during the first postoperative year. This discrepancy hinders comprehensive

understanding of the progression of rehabilitation and the early adaptations that ensue following musculoskeletal tumor resection.

Given these premises, the present doctoral project aims at filling these gaps following different steps:

1.The first step, which coincides with the first aim of this project, is a general characterization of the pre-operation gait and balance patterns of patients suffering of bone/muscles tumor/sarcomas. Characterization will be obtained through an ecologic approach based on a combination of wearable inertial measurement units (IMUs) and functional motor tests. The purpose is to provide clinicians with information useful in the programming of surgical treatments, and it might provide significant information which can be used at the time of post-surgical rehabilitation.

2. The second step will describe the progression of the rehabilitation process in sarcoma patients undergoing surgery at the lower limbs and lower back. Patients will be tested preoperatively (T0), at 3 months (T1), at 6 months (T2), and 1 year (T3) after the intervention.

Several innovative elements can be pointed out: first of all, the important ecological impact obtained by the un-obtrusive and wearable evaluation. The use of inertial sensors for clinical assessments is, in fact, an upward trend. Technological advancements in the gait and balance measurements led to the development of wearable technologies, such as IMUs, which allow to step outside the environment of a laboratory of human movement analysis, giving the chance to test patients in a more ecological environment. User-friendly, easy to wear, and portable, IMUs can be easily integrated in the clinical routine and used also by clinicians without a specific biomechanical expertise. Although IMUs are currently consistently widespread, the present project would be the first clinical application in the functional evaluation of sarcoma patients post-operatively and throughout their recovery.

Another innovative aspect brought by the present project is an evaluation protocol based on a set of multiple functional tests, which better reflects patient's movements in everyday life. Limiting the assessments to just the analysis of linear gait, as it happens in most of the studies of the present literature review, might not give sufficient information on the patient's functional state or recovery. For example, the 2-minute walking test might provide more accurate information on the patient's adaptations during prolonged walking, rather than a simple linear gate test performed on a few-meter walkway, as generally done in most of the

studies. A balance task might add information on the patient's upright posture and the risk of falls, and the Timed Up and Go test might describe the patient's ability to perform a common daily activity such as getting up from a chair or get around an obstacle. In this way, clinicians might have a detailed description of the patient's ability to return to active daily living.

A clear advantage of the proposed approach is represented by its full portability that opens to the possibility to perform outdoor free living assessments. This will be also fostered by the type of motor tasks that are typical of activities of daily living, as above mentioned.
This aspect is of great interest in the context of telemedicine whereas the clinicians is interested in monitoring patient's behavior not only in controlled environments (lab, gym, hospitals) but above all in real-life contexts to favor the progressive patient's autonomy and full recovery.

The main studies conducted within the present Ph.D. project are performed within a wider project named "Movement analysis in musculoskeletal oncology: a pilot study", promoted by IFO-IRE *Istituto Nazionale Tumori Regina Elena* in partnership with the University of Rome "Foro Italico". The study is a non-interventional, prospective, multicenter pilot study conducted on patients with primary and secondary tumors of the musculoskeletal system and has been designed to investigate the effects of the therapy, using both subjective and objective movement analysis detection techniques.

2.6 Design of the Functional Assessment Protocol

An accurate assessment of motor function constitutes a fundamental component of postoperative evaluation and rehabilitation in orthopedic patients. Quantitative and objective evaluation tools enable clinicians and researchers to monitor recovery trajectories, identify functional impairments, and assess the effectiveness of interventions. As stated in the previous chapter, conventional clinical scales and observational assessments, despite their extensive utilization, are frequently constrained by subjectivity and ceiling effects. To overcome these limitations, the present PhD study adopted an instrumented functional assessment protocol integrating wearable inertial measurement units (IMUs).

In the course of establishing the tumor patient's evaluation protocol of the present PhD study and defining the methods of administration based on the findings of available literature, functional tests specific for patients who have undergone surgery on the lower limb and lower back were identified. Following the example of the evaluation protocol suggested by Basteck et al. (2022) and Furtado et al. (2020), the patient evaluation protocol utilized in the present PhD study encompassed three distinct components: the 2-minute Walking Test (2MWT), performed as a linear gait at a self-selected speed for two minutes, to assess patients' walking abilities; secondly the instrumented Timed Up and Go (TUG), to assess patients' functional abilities which resemble some of the common movements performed in the daily living; posturography, to assess patients' balance control.

The tests have the capacity to detect clinically meaningful improvements in walking abilities in both healthy and clinical populations (Valeria Belluscio et al., 2019; V. Belluscio et al., 2019; Bohannon et al., 2015; Yang et al., n.d.), and all the assessments can be performed in standard clinical environments with minimal patient risk, even in post-surgical phases (American Thoracic Society, 2002; Butland et al., 1982). Moreover, the utilization of wearable inertial measurement units (IMUs) facilitates comprehensive motion analysis that surpasses conventional time- or distance-based metrics, thereby conferring advanced biomechanical insight.

Each test is designed to assess a distinct yet interconnected domain of motor function, namely gait performance in prolonged walking, mobility, and postural control. Collectively, these domains are able to provide a comprehensive evaluation of functional recovery.

Test	**Functional Domain**	**IMU-Derived Parameters**
2MWT (instrumented)	Endurance, gait performance	Gait speed, step length, cadence, support phase duration
iTUG	Functional mobility, dynamic balance	Sit-to-stand duration, turning time, total time
Posturography	Static balance, postural control	Sway area, sway velocity, frequency components

The 2MWT is a submaximal functional test that measures the distance an individual can walk in two minutes. It is traditionally used to assess walking endurance and capacity (Butland et al., 1982). While the test was originally developed as a clinical measure that only

necessitated the use of a stopwatch and distance markers, its value is amplified when instrumented with Inertial Measurement Units (IMUs). Positioned on the lower limbs and trunk, they can record spatio-temporal parameters of gait (Muro-de-la-Herran et al., 2014). This configuration enables the extraction of detailed metrics, including but not limited to average walking speed, step length, cadence, stride duration, and inter-limb symmetry.

The Timed Up and Go (TUG) test is a clinical evaluation tool that assesses functional mobility by measuring the time it takes to complete a series of everyday motor tasks. These tasks include rising from a seated position, walking a distance of three meters, turning, and returning to a seated position (Podsiadlo and Richardson, 1991). The total completion time has been demonstrated to provide a general indicator of mobility and fall risk. However, when augmented with IMU-based analysis (iTUG), the test facilitates the subdivision of each phase and the detailed assessment of dynamic transitions (Ortega-Bastidas et al., 2023). The evaluation involves the analysis of dynamic balance and mobility strategies across multiple postural transitions. The test demonstrates sensitivity to subtle motor deficits, which are not discernible through the analysis of total completion time alone and provides complementary data to the 2MWT by focusing on shorter, more complex movement sequences. Reliability was demonstrated in oncologic orthopedic populations (Furtado et al., 2020).

Posturography is a quantitative assessment tool that quantifies an individual's ability to maintain an upright stance under both static and perturbed conditions. When conducted using IMUs, posturography provides an accessible alternative to force-platform measurements, enabling estimation of center-of-mass sway through trunk acceleration data (Mancini et al., 2012). A single IMU positioned on the lower back can be utilized to record acceleration signals during quiet standing, both with eyes open and with eyes closed. Derived parameters include sway area, mean velocity, and frequency characteristics of postural oscillations.
This clinical test allows to assess the postural stability and sensory integration capabilities of the subject by the isolation of the control of balance under minimal movement. Also, this test demonstrates sensitivity to subtle deficits in proprioceptive or neuromuscular control that may persist after orthopedic surgery (Furtado et al., 2020).

The integration of these three IMU-based assessments ensures a multidimensional characterization of functional performance. Each test is designed to assess a specific domain

of motor function, and when considered collectively, they provide a comprehensive description of the motor function continuum: the 2MWT as a measurement of walking performance, the iTUG model as a framework that incorporates transitional mobility and dynamic balance, and the posturography test as a measure of static balance and postural control. The assessment protocol was designed to require approximately 20–25 minutes per subject, making it compatible with outpatient follow-up sessions, thus making it easy to reproduce and apply in a clinical setting.

By employing wearable sensor technology, this protocol enhances the precision and reproducibility of clinical assessment, thereby bridging the gap between traditional observation-based methods and advanced motion analysis. Such an approach enables clinicians and researchers to capture subtle changes in functional ability, track longitudinal progress, and objectively evaluate rehabilitation outcomes, ultimately contributing to more personalized and evidence-based orthopedic care.

Nonetheless, the implementation of the protocol in a clinical environment necessitated methodological adaptations to address spatial and logistical constraints. The execution of the instrumented 2-Minute Walk Test was particularly affected by the limited space available in the assessment area, which did not meet the distance requirements specified in the standardized guidelines (American Thoracic Society, 2002). These guidelines necessitate a minimum spatial requirement of 30m to ensure optimal performance and to obtain results that closely resemble the patient's actual data. Therefore, a methodological study, described in the following chapter, was conducted to elucidate the effects and feasibility of performing this test in a space smaller than recommended.

Chapter 3 – Methodological Study

Impact of walking path length on gait parameters during the 2-minute walk test in healthy young adults

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Abstract

Background/Objectives: The 2-minute walk test (2MWT) is a time-based gait assessment commonly employed for populations with limited walking ability for greater tolerability compared to the longer 6-minute test. The recommended distance to perform the tests is a 30 m straight path, a space requirement that is not always available in non-laboratory contexts. Shorter paths are therefore often adopted, but associated changes in gait patterns are not clear. The aim of the study is therefore to investigate how different walking path lengths affect gait patterns during the 2MWT. *Methods:* Twenty healthy young adults performed three walking trials on a straight hallway of 5 m, 15 m, and 30 m lengths. Spatiotemporal gait parameters were measured using three inertial measurement units on both distal tibiae and at pelvis level. *Results:* The 5 m path showed the greatest deviations, specifically in walking distance, walking speed, stride duration, stance time, swing time, single support time, and cadence, if compared to longer distances ($p < 0.05$). The 15 m path showed differences only in walking distance and walking speed ($p < 0.05$), if compared to the 30 m path. *Conclusions:* Shorter path lengths, particularly the 5 m, significantly impact gait patterns and should be considered when interpreting 2MWT results in clinical settings. The 30 m path is recommended as the gold standard, with 15 m as a viable alternative for assessing temporal parameters. Nevertheless, the extent to which each feature would be over/underestimated when walking in limited spaces is also addressed.

3.1 Introduction

Human walking is a complex motor function, integrating the motor and sensory systems (American Thoracic Society, 2002; Hollman et al., 2011). To evaluate walking performance and estimate health status across populations, time-based tests like the 12-Minute Walk Test, and distance-based tests like the 10-Meter Walk Test, are commonly used. Shorter versions of time-based tests, such as the 6-Minute Walk Test (6MWT) and 2-Minute Walk Test (2MWT), are highly correlated with longer versions (Butland et al., 1982). The 6MWT is popular due to its simplicity and similarity to daily living activities. However, for individuals with walking difficulties, such as amputees or frail elderly, the 2MWT is preferred for its better tolerability and safety (Chan and Pin, 2020; Frlan-Vrgoc et al., 2011; O'Keefe et al., 2021; Wafi et al., 2023; Wong et al., 2020).

In time-based tests assessing functional capacity, total walking distance and walking speed are the most commonly measured parameters. More recently, wearable devices, like inertial measurement units (IMUs,) have been used for instrumenting different tests allowing to capture spatiotemporal gait parameters, upper body accelerations, and gait variability, either in clinical or real-life settings (Grimpampi et al., 2015; Kushioka et al., 2022; O'Keefe et al., 2021; Theunissen et al., 2023; Wang et al., 2015). Guidelines for the 6MWT recommend a straight path of at least 30m to minimize turning points and maximize the distance walked (American Thoracic Society, 2002).

However, such space may not always be available in clinical settings, thus motivating studies aimed to explore the feasibility of adopting shorter paths, such as 5m, 10m, 15m, and 20m (Lipkin et al., 1986; Troosters et al., 1999). Barnett et al. (2016) compared the execution of the 6MWT across different path lengths and configurations (5m, 10m, 15m, 30m, rectangular, and continuous figure-of-eight), finding differences in walking speed, distance, and variability in stride length, stride width, and stride time, especially in shorter paths like 5m.

Since the 6MWT can be time-consuming and fatiguing, especially for patients with walking impairments, the 2MWT has been adopted as a shorter and tolerable alternative (Gaunaurd et al., 2020). Despite the recommendation of 30m straight path for the 2MWT (Pin, 2014), shorter or more discontinuous paths are often used in clinical environments. A recent study (Shank et al., 2022) compared 2MWT performance across six clinical settings with varying path lengths, obstacles, and surfaces. Results showed significant differences in total walking distance compared to normative reference values of research laboratory studies, indicating

the impact of environmental factors. However, the study did not explore spatiotemporal gait parameters, leaving a gap in understanding how short path lengths influence gait patterns. Thus, to the author's knowledge, there is no clear indication in the literature as to the extent to which different gait parameters change because of shorter path lengths. An enhanced understanding of how much gait patterns are under-/overestimated when performing shorter paths could be informative for guiding the choice of optimal settings for administering gait test protocols and for better interpreting the results when these settings are unavailable. Hence, this study aims to determine if and how manipulations in walking path length would affect 2MWT gait patterns in healthy adult individuals.

3.2 Methods

Twenty healthy young adults (10 males and 10 females; mean age: 27.3 ± 2.9 years; body mass index BMI: 22.8±2.4 kg/m2) were recruited (Power Analysis, G*Power: effect size f = 0.4, power (1-β error = 0.95, α = 0.05)) for this cross-sectional study. Exclusion criteria were psychological, neurological, musculoskeletal disorders, or any condition affecting gait, and injuries occurred in the last six months.

Participants performed three 2MWT trials, one for each straight paths of 5m, 15m, and 30m in a randomized order. A rest period of at least 3 minutes was provided between trials, and participants were asked whether they felt ready to continue before starting the next trial. Participants were instructed to walk at their normal, self-selected pace, wearing comfortable shoes. Turning points (180°) were marked at the ends of each path (Figure 2b), and verbal cues were used to signal the start and stop of each trial. Three synchronized IMUs (Movit® by Captiks Srl, Rome, Italy, 100Hz, ±1.7 g range) were placed on both lateral distal tibiae and at L5 level (Figure 2a). Sensors were secured using Velcro straps and positioned according to the manufacturer's guidelines.

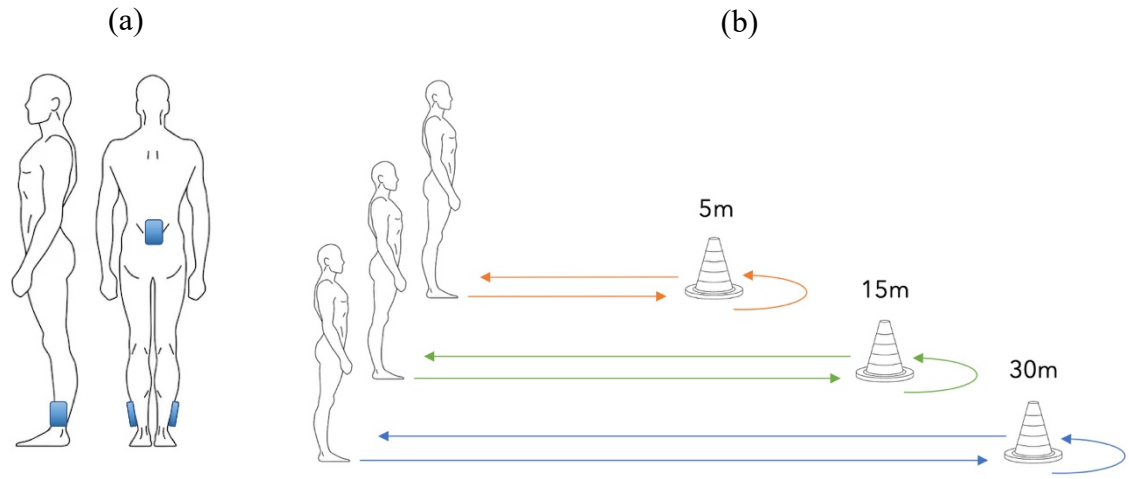

Figure 2 *– Illustration of the experimental setup: (a) Schematic representation of the placement of the inertial sensors (Movit®, Captiks Srl, Rome, Italy) on both lateral distal tibiae and at the L5 level; (b) schematic representation of the walking paths used in the 2-minute walk test (5 m, 15 m, and 30 m), with cones marking the turning points (180° turns).*

Raw accelerometer and gyroscope data were processed with the manufacturer's validated algorithms using Motion Analyzer software (Captiks srl) which automatically detects gait events and compute spatio-temporal parameters. The validity and reliability of these algorithms for spatio-temporal gait analysis have been previously reported (Ricci et al., 2019; Saggio et al., 2021). The following gait parameters were extracted: walking distance (WD) (m), walking speed (WS) (m/s), cadence (steps/min), stride duration (s), double support time (s), single support time (s), stance and swing phases (s).

Statistical analyses were conducted in SPSS Version 29 (IBM Corporation) using repeated measures ANOVA for normally distributed data and Friedman tests for non-normally distributed data. Post-hoc comparisons employed Bonferroni correction, to prevent Type I error. Effect sizes for each comparison were expressed as $\eta\rho^2$ values.

3.3 Results

Each of the 20 participants completed all three trials, resulting in a consistent dataset size across all conditions. Results are summarized in Table 2, highlighting significant differences across the three path lengths. WD for the 5m path was significantly lower compared to both the 15m and 30m paths ($p<0.001$), and the 15m path also showed a significant reduction compared to the 30m path ($p<0.001$). Similarly, WS also differed across all path lengths,

with the 5m path showing the largest reduction ($p<0.001$ for 5m vs. 15m/30m; $p=0.005$ for 15m vs. 30m). Other gait parameters (cadence, stride duration, double support time, single support time, stance, and swing time) showed no significant differences between 15m and 30m paths. In contrast, the 5m path led to increased stride duration, swing time, single support time, accompanied by a decrease in cadence ($p\leq0.001$). Stance time (significant in the main effect but not in post-hoc comparisons) and double support time showed no significant differences. Table 3 reports the extent of underestimation or overestimation of each parameter for the 5m and 15m paths relative to the 30m path. WD and WS appear to be the most affected by shorter paths, whereas stride-level temporal parameters remain largely consistent for 15m. The 5m configuration, instead, showed an overestimation of stride duration, swing time, and single support time, and an underestimation of cadence.

Table 2 *- The groups mean and standard deviation (SD) of each parameter for each straight-line walking length are reported. The p-value of each main effect is reported, and bold numbers indicate statistically significant differences ($p<0.05$). Effect size is reported as Eta-squared ($\eta\rho2$), for parametric tests, or Kendall W (W), for non-parametric tests.*

	5m		**15m**		**30m**			
	Mean	± SD	Mean	± SD	Mean	± SD	P-value	Effect Size
Walking Distance (m)	123.69 [a,b]	14.36	161.77 [a,c]	14.67	179.37 [b,c]	19.42	**<0.001**	$\eta\rho^2 = 0.952$
Walking Speed (m/s)	1.62 [a,b]	0.17	1.69 [a,c]	0.16	1.76 [b,c]	0.16	**<0.001**	W = 0.473
Stride Duration (s)	1.05 [a,b]	0.07	1.01	0.06	1.00	0.06	**<0.001**	$\eta\rho^2 = 0.625$
Stance Time (s)	0.61	0.06	0.60	0.05	0.59	0.05	**0.01**	$\eta\rho^2 = 0.268$
Swing Time (s)	0.43 [a,b]	0.03	0.41	0.02	0.41	0.02	**<0.001**	$\eta\rho^2 = 0.561$
Single Support Time (s)	0.42 [a,b]	0.02	0.41	0.02	0.41	0.02	**<0.001**	$\eta\rho^2 = 0.508$
Double Support Time (s)	0.19	0.05	0.19	0.04	0,18	0,04	0.265	$\eta\rho^2 = 0.067$
Cadence (steps/min)	115.48 [a,b]	7.30	119.05	6.66	119.97	6.76	**<0.001**	$\eta\rho^2 = 0.658$

a Significant difference from 30m.

b Significant difference from 15m.

c Significant difference from 5m.

Table 3 *- The underestimation level of each parameter is reported as a difference expressed in their respec-tive measurement units (left part of the table) and then expressed as a % difference (right part of the table).* ***Bold*** *values indicate measurements that were found to be statistically significant in Table 1.*

	Underestimation level of:			Difference (%)		
	5m compared to 15m	**5m compared to 30m**	**15m compared to 30m**	**5m compared to 15m**	**5m compared to 30m**	**15m compared to 30m**
Walking Distance (m)	**-38.07**	**-55.68**	**-17.61**	**-23.5%**	**-31.0%**	**-9.8%**
Walking Speed (m/s)	**-0.06**	**-0.14**	**-0.07**	**-3.7%**	**-7.8%**	**-4.2%**
Stride Duration (s)	**0.03**	**0.04**	0.01	**3.3%**	**4.1%**	0.8%
Stance Time (s)	0.01	0.02	0.01	2.1%	3.1%	1.0%
Swing Time (s)	**0.02**	**0.02**	0.00	**4.9%**	**5.5%**	0.5%
Single Support Time (s)	**0.01**	**0.01**	0.00	**2.3%**	**2.8%**	0.4%
Double Support Time (s)	0.00	0.01	0.00	1.6%	3.9%	2.3%
Cadence (steps/min)	**-3.57**	**-4.49**	-0.92	**-3.0%**	**-3.7%**	-0.8%

3.4 Discussion

This study aimed to assess the impact of path length on 2MWT gait parameters in young adults. Results show that walking path length significantly affects 2MWT performance, with shorter paths leading to reductions in WD and WS, as well as alterations in temporal parameters. These findings are consistent with previous studies on the 6MWT (Barnett et al., 2016), suggesting the adoption of different walking strategies on shorter paths. In addition, considering the range of values obtained for each gait parameter in this study, it was possible to indicate the extent to which each feature would be over/underestimated when walking in limited spaces (Table 3).

The highest WD and WS values were observed on the longest walking path (30m), followed by the 15m path, with the lowest values recorded for the 5m path. Specifically, WD on the 5m path was 31% lower than the gold standard 30m path, while the 15m path showed a reduction of over 23%. This aligns with previous findings about the 6MWT (Barnett et al., 2016), demonstrating that reducing the number of required turns significantly improves total walking distance in the 2MWT. Additionally, longer uninterrupted walking allows participants to reach a steady-state WS, minimizing the impact of acceleration and deceleration phases, which are usually around 2.17m each (Middleton et al., 2015). In the 5m path, most of the distance comprises these phases, resulting in lower WS. Since WS is a functional vital sign and a predictor of health status, clinicians should carefully consider path length effects, as a reduction from 30m to 5m leads to an 8% drop in WS (Table 3). Regarding

the clinical significance of such percentage variations, the differences in walking speed observed between the 15 m and 30 m paths (0.07 m/s) remain below or at the lower bound of minimal clinically important differences (MCID) reported in adults with various pathologies, which range from 0.10 to 0.20 m/s (Bohannon and Glenney, 2014). We cannot state the same for the differences between 5 m and 15 m, which amount to 0.14 m/s, appearing clinically relevant. This suggests that, for the 15 m walkway, the difference in total walking distance com-pared to the 30 m path (approximately 18 m) may be clinically meaningful in certain patient populations, such as those in subacute stroke or undergoing COPD rehabilitation (Johnston et al., 2017), while it may not be relevant for others (Bowman et al., 2025). Overall, our findings indicate that, for a 15 m walkway, all stride-level temporal parameters can be reliably measured, while deviations in walking speed are minimal and unlikely to be clinically meaningful. For the WD, instead, the 15 m walkway should be interpreted with caution, as the clinical significance of this difference should be considered relative to the patient's pathology.

For temporal parameters, results showed an inverse relationship with WS, consistent with prior studies (Smith and Lemaire, 2018; Ziegler et al., 2024). The 5m path produced the greatest temporal alterations, while the 15m and 30m paths showed no significant differences. Stride duration was longest on the 5m path, likely due to the slower WS, as previously reported (Smith and Lemaire, 2018; Ziegler et al., 2024), where both studies observed an increase in the stride duration when reducing walking speeds. The slower WS also affected stance and swing time. However, in this study, while stance and swing time were both longer on the 5m path, only swing time differences were statistically significant from 15m and 30m paths, with a swing increase of over 5% and single limb support time increase of nearly 3% when reducing the path length from 30m to 5m (Table 3). As previously stated, instead, the stance duration and the double support time did not show significant differences. The lack of significant stance time alterations supports the idea that stance and swing relate to distinct control mechanisms (Smith and Lemaire, 2018): stance time appears to vary linearly with WS, while swing relation to WS seems to be better rep-resented by a polynomial quadratic model, meaning the relation between the decrement of the swing value at the increment of the WS is not represented by a straight line but follows a quadratic function. Additionally, it should be considered that walking over 5m mainly consists of acceleration/deceleration phases, rather than steady state walking. Thus, it is suggested that these phases may involve different walking strategies and their influence on gait temporal parameters would require further investigation.

In terms of cadence, the 30m and 15m paths produced values consistent with those previously reported in the 6MWT (Kushioka et al., 2022). Cadence decreased by about 3% in the 5m path compared to the 30m path (Table 3), consistent with the longer stride duration and supporting the correlation between cadence and WS previously reported (Retory et al., 2019).

To the author's knowledge, this study represents the first attempt to quantify how walking path length influences gait patterns in the 2MWT for young adults, and how much gait parameters are under- or overestimated when performing the 2MWT on shorter paths than the recommended 30m.

From a practical perspective, these findings have direct clinical implications. Specifically, an underestimation of the walking speed due to a shorter path length could lead to misclassification of a patient against established cut-off values used for risk stratification, despite their actual performance being adequate. Similarly, underestimations in total walking distance of up to 30%, or smaller but systematic deviations in cadence and stride duration could lead to incorrect interpretations of functional capacity or rehabilitation progress. Reporting both raw and percentage differences, as provided in this study, facilitates a more accurate adjustment of test results when the recommended 30 m walkway is not available. Recognizing the systematic underestimation introduced by shorter walkways can support clinical decision-making in different scenarios, such as when comparing patient outcomes across facilities with varying space availability, when monitoring progress in rehabilitation programs, or when interpreting longitudinal changes in patients tested in different environments.

In these conditions, understanding the levels of under-overestimation in investigated gait parameters, especially those resulting from the interaction of various factors including body structure, postural control, lower extremity strength, and proprioception (Middleton et al., 2015), can be valuable for clinicians. Addressing these under-overestimations can improve the accuracy of test results, allowing for more reliable comparisons with normative values obtained under standard conditions. Furthermore, accurate measurements are crucial for evaluating patients effectively and determining whether there are impairments in any of the systems that contribute to human walking.

Some limitations must be addressed, such as the focus on only young adults. Other individual factors, including age, BMI, and the presence of gait impairments, are known to affect spatiotemporal parameters and may interact with walkway length.

3.5 Conclusions

When assessing gait spatiotemporal parameters, the 30m path should be considered the gold standard, while the 15m path might represent a suitable alternative. In this condition, walking speed is slightly underestimated on shorter paths, but the magnitude of this change is unlikely to be clinically meaningful, and temporal parameters such as cadence, stride duration, stance, and swing times, showed minimal differences between 15 m and 30 m paths, supporting the acceptability of these measures even when dealing with shorter walkways. In contrast, total walking distance is more strongly affected by path length. Therefore, clinicians may consider using a 15 m walkway when a 30 m space is unavailable.

The 5m path appears to be the least preferable, as short paths do not allow for steady-state walking speed and may introduce compensatory strategies. However, if an appropriate quantity of space is not available, as in clinical environments, it is essential to consider the impact of shorter distances on gait patterns, the extent of underestimation of specific parameters and adjust interpretations accordingly.

For future research, further studies are needed to extend the analysis to more heterogeneous cohorts, including elderly populations and clinical groups with gait impairments, to confirm whether the findings observed in healthy young adults generalize to these populations.

Chapter 4 – Preoperative Assessment and Patient Differentiation

Preoperative motor function in patients with lower limb tumor patients: influence of tumor type and size

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Abstract

Background: Musculoskeletal tumors can significantly affect motor function, yet preoperative functional status is poorly characterized. Understanding baseline motor abilities is crucial for guiding surgical planning, rehabilitation, and risk assessment. Purposes: This study aimed to investigate whether and how bone/soft tissue tumors alters gait and functional abilities at the preoperative stage. Additionally, we explored whether tumor volume is associated with specific motor impairments. *Methods:* Sixty-five participants were included: 17 with bone tumors (BT), 27 with soft tissue tumors (STT), and 21 healthy controls (HC). Participants performed a 2-minute walking test, Timed Up&Go (TUG) test, and static balance assessment using 15 wearable inertial sensors in a clinical setting. Spatiotemporal gait parameters, TUG subcomponents, postural sway, pain level while walking, and tumor volume were analyzed. *Results:* Both BT and STT patients exhibited reduced gait speed. Also, BT showed altered stance, swing, and double support phases compared to healthy controls. Turn duration during TUG was significantly higher in both tumor groups ($p < 0.001$), while static balance parameters were similar across groups ($p>0.05$). Tumor volume was moderately correlated with stand-to-sit lean angle in BT ($r = 0.503$) but not with other parameters. Pain scores were higher in BT than in STT ($p < 0.001$). *Conclusion:* Preoperative motor function is compromised in patients with musculoskeletal tumors, particularly bone tumors, affecting gait and complex mobility tasks but not static balance. Wearable inertial sensors provide objective, ecologically valid assessments that can guide targeted prehabilitation, risk stratification, and individualized care.

4.1 Introduction

The treatment of musculoskeletal tumors, including both bone and soft tissue tumors, typically involves a multidisciplinary approach combining surgery, chemotherapy, and radiotherapy, depending on tumor type, grade, and stage (Grünewald et al., 2020). Surgical interventions are often highly invasive and may vary depending on the type of tumor, possible different types of prosthetic implantation (Benedetti et al., 2013; Kim et al., 2021a; Pesenti et al., 2018), as well as the level of resection or excision and specific muscles removed (Benedetti et al., 2000; Bozkurt et al., 2005). However, to date, while much focus has been placed on postoperative functional impairments, little is known about patients' motor status before treatment, limiting interpretation of surgical outcomes. Of particular relevance is the fact that the nature of this disease results in a patient population which is notoriously heterogeneous in tumor features, such as size, growth rate, and anatomical location (Sbaraglia et al., 2021), and, as said, in the corresponding surgical interventions. This clinical variability throughout the treatment pathway underscores the need for objective functional assessment protocols, essential for guiding truly individualized rehabilitation strategies and monitoring surgical success, in the corresponding surgical interventions. In fact, surgery, regardless of the specific procedure performed, may result in significant changes in motor function, with alterations in gait patterns, (National Cancer Institute, 2025), including reductions in spatiotemporal parameters such as gait velocity, stride length, and cadence, along with longer stride durations (Filis et al., 2022). Also, in terms of postural performance, poorer balance was displayed by tumor survivors compared to healthy controls (Furtado et al., 2017).

Therefore, characterizing preoperative motor function may offer key clinical benefits and complements postoperative evaluations. Establishing baseline motor status aids in accurately interpreting postoperative changes, tailoring surgery and rehabilitation, but also identifying pre- and post-operative deficits that may increase risks such as falls.

Another key point to consider is the assessment tools used to quantify motor function. In routine clinical care, functional evaluations often rely on subjective questionnaires, which may lack precision (Kask et al., 2019). Objective data from functional assessments are available in the literature – despite nearly all reviewed studies on this population limit assessments to straight-line walking tasks, sometimes at varying speeds (Jaegers et al., 1995; Okita et al., 2014a), which may not fully capture the complexity of functional mobility in daily life. To overcome this limitation, wearable technologies, particularly inertial

measurement units (IMUs), have emerged as reliable, portable, and low-invasive tools for capturing detailed movement data in diverse clinical populations (Iosa et al., 2016). Their ease of use outside laboratory settings allows for assessments in more ecological and accessible environments.

Rationale: Understanding preoperative motor status could enhance clinical decision-making, support rehabilitation and prehabilitation planning, and serve as a screening tool to identify risk factors such as fall risk (Verghese et al., 2009). Furthermore, there is the need to quantify motor deficits, overcoming clinical qualitative evaluations. Therefore, this study aims to investigate whether, and to what extent, tumor presence and size affect gait and functional abilities preoperatively in patients with tumor lesions, using an ecological and objective evaluation protocol based on wearable inertial sensors.

4.2 Methods

Study Population

An observational, cross-sectional framework was adopted for this research. The study included a total of 65 participants: 17 patients diagnosed with bone tumor (BT), 27 diagnosed with soft tissue tumors (STT), and 21 healthy controls (HC). The sample size was determined based on a priori power analysis (G*Power) using pilot data: effect size f =0.4, power (1-β error = 0.8, α = 0.05).

Participants were eligible if they met the following criteria: 1) age ≥ 16 years; 2) diagnosis of a musculoskeletal tumor through biopsy; 3) presence of a tumor localized in the lower limb or lower back; 4) candidates for surgical intervention involving bone resection or excision of soft tissue lesions; 5) ability to ambulate independently, without assistive devices; 7) written informed consent.

The study was approved by the Central Ethics Committee of Istituto di Ricovero e Cura a Carattere Scientifico (I.R.C.C.S.) Lazio – I.R.C.C.S I.F.O. (Clinical Trial Register No. 1704/22).

Experimental Protocol

All assessments were conducted at the time of hospital admission at the IFO IRE Regina Elena Institute in Rome.

After clinical screening, patients were equipped with a set of 6 wearable sensors (OPAL, APDM Inc.) with a sampling frequency of 128Hz. Sensors were placed on sternum, lower back, feet, forearms. Participants performed the following motor tasks: *i)* a 2-minute walking test (2MWT) (Butland et al., 1982; Pin, 2014), where were asked to walk back and forth along a 12 m straight path for 2 minutes at a self-selected speed; *ii)* three instrumented Timed Up and Go (iTUG) test (Kleiner et al., 2018; Podsiadlo and Richardson, 1991), where participants started seated in a standard height chair, stood up, walked 3 meters, turned around, returned to the chair, and sat down; *iii)* a static bipodal balance task, where participants stood still for 30 seconds, maintaining a natural stance while fixing a point on the wall at the level of their eyes (Mancini et al., 2012). While the iTUG and static balance tests were completed in a randomized order, the 2MWT was always conducted at the end to prevent fatigue from affecting performance on the preceding assessments.

To assess pain perception during locomotion, a Numeric Rating Scale (NRS) ranging from 0 (no pain) to 10 (worst imaginable pain) was administered at the end of the 2MWT, in which participants were instructed to rate the intensity of the experienced pain while walking, providing a subjective measure of discomfort associated with the motor performance (Williamson and Hoggart, 2005).

Data collection and statistical analysis

Spatiotemporal gait parameters, iTUG duration and trunk kinematics, turn parameters, and sway parameters were assessed and processed with the Moveo Explorer® software through implemented algorithms (Fang et al., 2018; "How are Mobility Lab's algorithms validated? – Product Support And Information," n.d.; Monaghan et al., 2024; Morris et al., 2019). The following parameters for each motor task were extracted and interpreted taking into consideration the available limited walkway length (Lo Zoppo et al., 2025). *2MWT:* gait speed (m/s), cadence (steps/min) calculated as the mean between the two limbs; stance (%Gait Cycle Time - GCT), swing (%GCT), double support (%GCT) and stride length (m), calculated for both limbs, the one with tumor lesion (T) and the healthy limb (H). This approach was adopted to assess limb-specific parameters and allow for a more detailed characterization of compensatory strategies and functional impairments associated with the tumor, which might be masked when considering only global gait metrics. i*TUG:* total duration (s), turn duration (s), sit-to-stand duration (s), sit-to-stand lean angle (°), stand-to-sit duration (s), stand-to-sit lean angle (°). *Posturography:* sway area (m^2/s^4), Root Mean Square (RMS) sway (m^2/s^4), RMS coronal (m^2/s^4), RMS sagittal (m^2/s^4). Tumor volume

(cm^3) was estimated by approximating the mass as an ellipsoid and measuring its three semi-axes along the three principal axes length, width, and height from Magnetic Resonance Imaging with the supervision of an expert clinician (R.B.) (Dejaco et al., 2015). This measure was included to investigate the potential role of tumor volume in the observed changes of motor function. The $V = \frac{4}{3}\pi abc$, where a, b, and c are the three measured semi-axes along the three principal axes of the ellipsoid.

Data were analyzed using SPSS software Version 29 (IBM Corporation). For group differences, a One-Way ANOVA test for normally distributed data or Kruskal-Wallis test for non-normally distributed data were used. Post-hoc comparisons utilized Bonferroni correction or Wilcoxon tests to control the probability of a Type I error (false positive). Effect size for each comparison was expressed as η^2 (eta squared) values for normally distributed data, or ε^2 (epsilon squared) values for non-normally distributed data. Spearman correlation was used for exploring possible correlations between tumor volume and gait/postural parameters, and between pain level while walking and gait/postural parameters.

4.3 Results

When Demographic and clinical characteristics of 17 patients with bone tumors (BT) and 27 with soft tissue tumors (STT) are shown in Table 4. Twenty-one healthy controls (HC) were assessed as reference (mean age 40 years, range 15-73 years; 10 females). For the BT group, patients were diagnosed with chondrosarcoma (5), GCT (2), exostosis (2), osteosarcoma (3), chondromyxoid fibroma (1), chordoma (1), desmoplastic fibroma (1), enchondroma (1), Ewing's sarcoma (1). For the STT group, patients were diagnosed with lipoma (9 people), liposarcoma (6), myxofibrosarcoma (4), neurofibroma (2), pleomorphic sarcoma (2), synovial sarcoma (2), desmoplastic fibroblastoma (1), sacrococcygeal teratoma (1).

Table 4 *- Demographic characteristics of the sample. Age is expressed in years as mean (min–max); other values are presented as n. of cases and percentage (%) within each group.*

Group: BT	Patient characteristics	N = 17
	Age, mean (min-max)	47 (17-76)
	Female, n. (%)	11 (66)
	Site of the tumor, n. (%)	
	Pelvis	7 (41)
	Thigh	4 (24)
	Leg	5 (29)
	Foot	1 (6)
	Chemotherapy	1
	Radiotherapy	0

Group: STT	Patient characteristics	N = 27
	Age, mean (min-max)	56 (22-78)
	Female, n. (%)	18 (67)
	Site of the tumor, n. (%)	
	Pelvis	5 (19)
	Thigh	17 (63)
	Leg	4 (15)
	Foot	1 (4)
	Chemotherapy	2
	Radiotherapy	3

Motor task results are reported in Figure 3 and Table 5. In details:

2MWT: a significant main effect for group was found considering cadence ($p=0.04$, η^2 0.98) and gait speed ($p=0.016$, ε^2 0.13). For both tumor lesion limb and healthy limb, significant main effects were found for stance ($p=0.01$, η^2 0.14; $p=0.008$, η^2 0.14 respectively), swing ($p=0.01$, η^2 0.14; $p=0.008$, η^2 0.14 respectively), double support ($p=0.006$, η^2 0.15) and stride length ($p=0.043$, η^2 0.96; $p=0.034$, η^2 0.10 respectively). In the post-hoc pairwise comparison, no statistically significant differences were found between BT and STT, while several differences were identified when the two groups were compared with HC. More specifically, both BT and STT showed reduced gait speed ($p=0.01$ and $p=0.015$ respectively) with respect to healthy participants. Cadence and stride length were reduced in patient groups compared to healthy controls but showed no significant difference in the post-hoc pairwise comparison (both $p>0.017$). The BT group also showed for both tumor lesion limb and healthy limb a higher double support time (both $p=0.005$), increased stance time ($p=0.008$ and $p=0.007$ respectively) and reduced swing time ($p=0.008$ and $p=0.007$ respectively) compared to HC.

iTUG: a significant main effect was found among the three groups for iTUG duration and turn duration. In the post-hoc pairwise comparison no significant differences were observed

between BT and STT, while a statistically significant difference was in the turn duration, with both BT and STT showing a significantly higher turn duration compared to HC ($p < 0.001$). TUG duration was higher in the two patients group compared with healthy controls but showed no significant difference in the post-hoc pairwise comparison. Turn angle, sit-to-stand and stand-to-sit durations and angles did not show significant differences among the three groups ($p>0.05$).

Posturography: No statistically significant differences were observed across groups for sway area, RMS sway, or RMS coronal and RMS sagittal plane values ($p > 0.05$).

Pain: the pain score (NRS) showed a highly significant difference between the BT and ST groups ($p < 0.001$), with BT patients reporting the highest levels of pain (mean ± standard deviation = 5.17 ± 3.35).

Correlations: Spearman correlation analyses revealed a significant moderate positive correlation between tumor volume and stand-to-sit lean angle ($r = 0.503$) in the BT group. No significant correlations were found between tumor size and all the other analyzed parameters, and between pain level while walking and all the other analyzed parameters.

Demographic and clinical characteristics of 17 patients with bone tumors (BT) and 27 with soft tissue tumors (STT) are shown in Table 1. Twenty-one healthy controls (HC) were assessed as reference (mean age 40 years, range 15-73 years; 10 females).

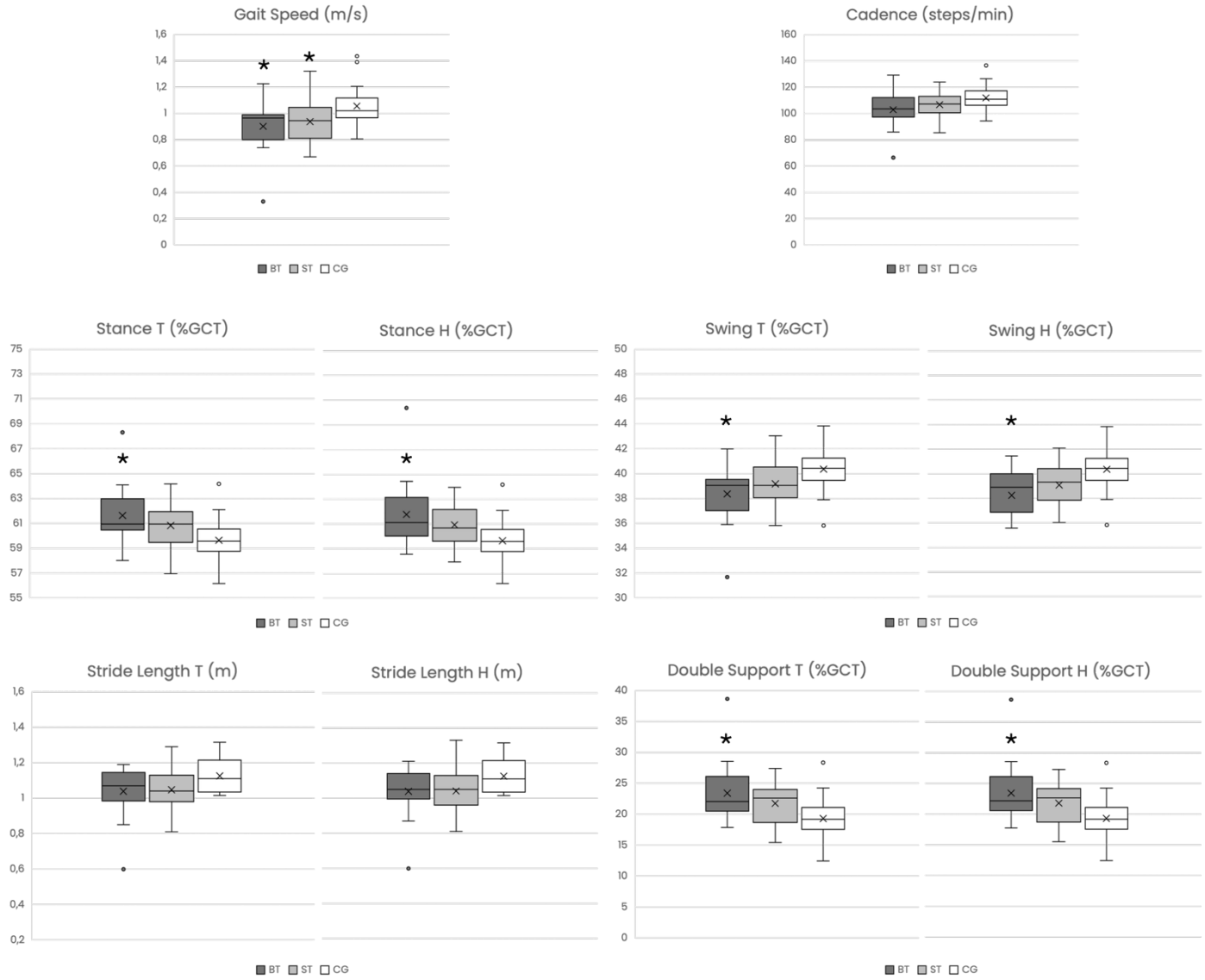

Figure 3 *– Figure reports boxplots showing the distribution of gait parameters across three groups: bone tumor (BT), soft tissue tumor (STT), and control group (HC). Asterisks * indicate statistically significant differences compared to the control group (HC).*

Table 5

*Table reports group mean and standard deviation (SD) of each parameter for each proposed motor task. P value of each main effect is reported, and **bold** numbers indicate statistically significant differences ($p<0.05$). Effect size is reported as Eta-squared (η^2) or Epsilon squared (ε^2). S: limb with sarcoma lesion, H: healthy limb, GCT: gait cycle time, RMS: root mean square. * Significant diff. from Control.*

	BT		**STT**		**HC**			
	Mean	±SD	Mean	±SD	Mean	±SD	p value	Effect Size
Timed Up&Go								
Duration (s)	12.29	3.71	12.86	2.27	10.84	1.24	**0.023**	η^2 0.11
Turn Angle (°)	177.77	8.96	178.32	7.00	176.68	9.18	0.791	η^2 0.01
Turn Duration (s)	**2.50***	0.53	**2.56***	0.35	2.07	0.39	**<0.001**	η^2 0.23
Sit-to-Stand Duration (s)	1.03	0.14	1.05	0.21	0.93	0.16	0.085	η^2 0.08
Sit-to-Stand Lean Angle (°)	26.87	10.46	24.75	8.51	22.49	9.93	0.223	ε^2 0.02
Stand-to-Sit Duration (s)	0.87	0.18	0.92	0.25	0.80	0.18	0.125	η^2 0.07
Stand-to-Sit Lean Angle (°)	27.43	11.46	21.45	9.02	23.21	10.08	0.234	ε^2 0.02
Posturography								
Sway Area (m^2/s^4)	0.01	0.01	0.02	0.01	0.01	0.01	0.291	ε^2 0.01
RMS Sway (m/s^2)	0.06	0.02	0.06	0.02	0.05	0.02	0.134	η^2 0.06
RMS Coronal (m/s^2)	0.01	0.01	0.02	0.01	0.01	0.01	0.392	η^2 0.03
RMS Sagittal (m/s^2)	0.06	0.02	0.06	0.02	0.05	0.02	0.195	η^2 0.051
Pain (NRS)	**5.17**	3.35	**0.82**	1.85	0	0	**<0.001**	ε^2 0.4

4.4 Discussion

The study aimed at investigating whether, and to what extent, the presence and size of the tumor affect gait and functional abilities in the preoperative phase of sarcoma patients. Results showed that patients with bone and soft tissue tumors exhibited alterations in gait pattern and functional abilities compared to healthy controls. Static balance parameters did not show notable group differences, while pain was more pronounced in the BT group.

Gait: Gait speed was found to be reduced in both groups of patients with tumors with respect to healthy participants.

Gait speed is widely recognized as a crucial indicator of functional mobility. Previous studies have shown that slower walking speeds tend to improve local dynamic stability - meaning that the gait becomes more resistant to small perturbations - when compared to faster speeds (England and Granata, 2007; Hyun G. Kang and Dingwell, 2008). However, reduced

walking speed is often associated with a decreased leg strength (Hyun Gu Kang and Dingwell, 2008) and greater likelihood of falls (Verghese et al., 2009).
In patients with tumors, these results seem to highlight the reduction in walking speed as a potentially compensatory strategy, which may serve to enhance stability. But also, it may reflect underlying motor impairment that contribute to an increased fall risk.

Furthermore, while patients with soft tissue tumors have been found gait patterns similar of those of the HC, suggesting that the presence of the tumor does not have an evident impact on the overall gait performance, patients with bone tumors exhibited several altered gait patterns. Specifically, BTs showed significantly longer double support time and stance phase duration, and a reduced swing phase duration compared to both healthy subjects and patients with soft tissue tumors, in both limbs.
The inverse relationship between gait speed and double support time is well documented: slower walking is associated with a longer double support phase, both in absolute duration and as a proportion of the gait cycle (Williams and Martin, 2019).
The altered gait characteristics observed in patients with bone tumors, including changes in double support and stance phases, may be related to decreased bone mineral density and compensatory strategies to maintain stability during walking (Horiuchi et al., 2023; Sung, 2018).
Besides, cadence did not show significant differences, although slightly lower than healthy subjects in both BT and ST groups, suggesting a preserved ability to maintain the rhythmic stepping patterns, especially in patients with bone tumors, despite the temporal alterations observed in other gait parameters. This may reflect a compensatory mechanism aimed at preserving gait regularity, even in the presence of biomechanical or neuromuscular impairments (Bacek et al., 2022).
iTUG: The total duration of the iTUG test did not reveal significant differences between patients with tumors and healthy controls. Similarly, no differences were found in the duration or trunk lean angle during sit-to-stand and stand-to-sit transitions. Interestingly, a more detailed analysis of the task's motor components showed that the turning phase (i.e., the curved walking segment) took longer to perform in both tumor groups compared to healthy subjects.
This is consistent with previous findings emphasizing the turning phase as particularly demanding and informative in functional assessments and supports the idea that phase-specific analysis provides a more accurate reflection of functional limitations (Mangano et

al., 2020). Also, this finding suggests difficulties in executing more complex motor tasks that require enhanced postural control and refined integration of balance, motor coordination, and movement planning systems (Belluscio et al., 2021; Chia Bejarano et al., 2017).

Static Balance: The presence of the tumor does not appear to significantly impair static balance control or its underlying mechanisms. Postural control is a complex, adaptive process that integrates somatosensory, visual, and vestibular inputs to achieve postural orientation (alignment of the body with gravity, support surfaces, and visual references) and postural equilibrium (stabilization of the center of mass against perturbations) (Horak, 2006). The findings of the present study may therefore suggest that, in the absence of specific sensory challenges, the integrated interplay of these systems is sufficient to preserve postural stability under eyes-opened, firm-surface condition, despite a localized pathological condition (de Visser et al., 2001; Karasimav et al., 2024). Moreover, since static and dynamic balance are known to deteriorate at different rates, with static balance generally remaining more preserved in conditions such as aging (Liaw et al., 2009; Lin et al., 2024), it is plausible that static balance control is not substantially compromised by the presence of the tumor. Further studies employing more challenging balance tests are required to fully assess potential subtle deficits.

Pain level during walking, measured as a self-reported outcome, was considerably higher in patients with bone tumors, compared with patients with soft tissue tumors.
Overall, bone tumors are associated with higher pain intensity and reduced physical functioning compared to soft tissue tumors, regardless of malignancy (Kruiswijk et al., 2023). Moreover, bone lesions can cause increased pain with weight-bearing and result in complications such as pathological fractures.

Correlations: Only for patients with bone tumors, a moderate positive correlation was found between tumor size and increased time required to complete the stand-to-sit phase. This phase involves precise muscular control and relies on eccentric contraction of the thigh extensor muscles (Jeon et al., 2021). Such impairment could possibly be influenced by the higher levels of pain reported by bone tumor patients, compared to those with soft tissue tumors. However, except for the aforementioned moderate positive correlation, tumor mass size does not appear to correlate with any of the gait, TUG, or static balance parameters.

This suggests that the size of the tumor is not the primary factor contributing to alterations in gait patterns or difficulties in performing complex motor tasks that require a higher level of postural and motor control. However, the stand-to-sit transition is a biomechanically demanding task, as it requires controlled eccentric contraction of the quadriceps and hip extensors to decelerate the body mass and ensure safe lowering to the chair. A slower execution of this movement may reflect the adoption of a protective strategy, aimed at minimizing instability and reducing the mechanical load placed on weakened or compromised musculoskeletal structures. Pain, also, could represent an additional factor contributing to the prolongation of the movement, as patients may unconsciously slow down the task to avoid discomfort or to better control potentially painful joint excursions.

From a clinical perspective, this study offers relevant insights into the preoperative functional abilities of patients with tumor lesions. By identifying specific gait and mobility alterations — particularly in bone tumor patients — it supports the utility of targeted prehabilitation strategies aimed at enhancing these functional deficits before surgical intervention. Moreover, the detection of phase-specific impairments in the TUG test underscores the importance of detailed functional assessments rather than relying solely on global scores. Such nuanced information may guide early interventions to mitigate fall risk, preserve autonomy and, ultimately, improving surgical outcomes and postoperative recovery. Also, these findings prompt further investigation into the role and functioning of muscular structures in the presence of a tumor, highlighting the need for detailed analysis of muscle function and activation patterns during gait in this specific patient group. In fact, tumor-induced systemic inflammation and metabolic competition may lead to early muscle impairment (Christensen et al., 2014).
Therefore, these results highlight the need for a multidisciplinary approach to tailor preoperative planning and rehabilitation programs.

Limitations and strength aspects of the study

One major strength is the novel focus on preoperative motor function in patients with musculoskeletal tumors, an understudied area in the literature. Understanding baseline functional status can provide a more complete clinical picture, support early risk stratification, and inform timely intervention strategies. Additionally, the inclusion of both bone and soft tissue tumor groups, alongside healthy controls, offers a comprehensive preoperative comparison across tumor types. Moreover, the use of wearable inertial sensors,

allowed for an objective, high-resolution assessment of gait and functional mobility in a real-world clinical setting. The ability to analyze specific motor subtasks, such as turning and transitions, provided detailed insights often missed by traditional global scores or subjective tools.

However, some limitations should be acknowledged. The sample size, though comparable to similar studies, remains relatively small, limiting generalizability. Furthermore, tumor lesions heterogeneity and high variability of the patients, both in terms of anatomical location and effects on functional outcomes, may also have influenced results, limiting detection of significant differences between the two patient groups. Additionally, static balance measures showed limited differences, suggesting the need for dynamic or more challenging balance assessments in future studies.

4.5 Conclusions

This study highlighted how the presence of musculoskeletal tumors, particularly bone tumors, significantly affects aspects of gait and functional mobility in the preoperative phase. The use of wearable inertial sensors enabled the detection of specific gait alterations undetectable through global assessments or subjective tools, highlighting their potential to bridge the gap between research and clinical practice by supporting ecological, repeatable, and easily integrable evaluation protocols in routine care.

Bone tumor patients showed more pronounced alterations in spatio-temporal gait parameters, likely as a compensatory strategy to maintain dynamic stability. These changes, together with higher reported pain levels and the observed correlation between tumor volume and difficulty in transitional movements, suggest a significant impact of the pathology on neuromuscular function and postural control during movement.

In contrast, patients with soft tissue tumors exhibited fewer alterations in gait and mobility, mainly limited to a reduction in walking speed, likely influenced more by possible systemic or muscle-related factors than by evident biomechanical deficits.

From a clinical perspective, the findings highlight the importance of integrating objective and granular functional assessments in the preoperative phase, in order to early identify those patients at higher risk of functional decline, falls, or postoperative complications.

In the future, a detailed understanding of preoperative functional status may guide targeted prehabilitation strategies, optimize multidisciplinary therapeutic planning, and, ideally,

improve surgical outcomes and postoperative recovery. Future studies conducted on larger cohorts and including postoperative follow-up will be essential to expand upon these findings, also incorporating the analysis of muscular function and more complex balance tasks through multimodal approaches.

Chapter 5 – Determinants of Postoperative Recovery: The Role of Preoperative Physical Activity

Influence of preoperative physical activity levels on postoperative recovery in patients with musculoskeletal tumors using wearable sensor-based functional assessment

(in preparation)

Abstract

Background: Physical activity (PA) can be beneficial in cancer management, improving quality of life, reducing treatment side effects, and enhancing functional recovery. While postoperative exercise is widely studied, the impact of preoperative PA on functional outcomes in oncological patients with musculoskeletal tumors remains underexplored. This study aimed to investigate whether a physically active lifestyle prior to oncologic surgery supports faster and more effective postoperative motor recovery. *Methods:* Twenty patients with bone or soft tissue tumors of the lower limbs or lower back were enrolled. Preoperative PA levels were assessed via questionnaire and categorized as active or sedentary. Functional assessments included the instrumented Timed Up and Go (TUG) test, static balance (Sway test), and the instrumented 2-Minute Walk Test (2MWT), captured using wearable inertial sensors. Within- and between-group comparisons were performed using appropriate parametric and non-parametric tests. *Results:* Eight patients were classified as active and 12 as sedentary. Within-group analyses showed stable motor performance in active patients, whereas sedentary patients exhibited postoperative changes in swing phase (healthy limb) and stride length (operated limb) during the 2MWT. Between-group analyses revealed significantly better postoperative performance in the active group for TUG turn duration, turn velocity, and 2MWT stride length for both limbs. No significant differences were observed in postural sway measures. *Conclusion:* Preoperative physical activity may exert a protective effect on motor function, facilitating more efficient postoperative recovery in oncological patients with musculoskeletal tumors, particularly in complex motor tasks requiring coordination and neuromuscular control.

5.1 Introduction

Physical activity is described as energy-demanding movement produced by skeletal muscles, occurring across leisure, occupational, and domestic domains (WHO, 2025a). In recent decades, a wide range of studies has demonstrated the crucial role of physical activity in the management of cancer patients, both during treatment and in the post-operative recovery phase. Scientific literature has highlighted that exercise not only significantly improves the quality of life of these patients but also helps reduce the side effects of oncological therapies, enhances muscular and cardiovascular function, and promotes faster recovery (Courneya et al., 2015). It is also evident that physical activity is associated with a decreased risk of developing various types of cancer, including colon, breast, prostate, and endometrial cancers (Jurdana, 2021). Benefits have also been observed in relation to cancer-related fatigue, demonstrating that exercise can reduce chronic fatigue, one of the most debilitating effects of oncological therapies, while improving patients' functional capacity (Schmitz et al., 2010). Moreover, supervised exercise programs appeared to generate benefits in muscle strength, endurance, and psychological well-being among patients undergoing cancer treatment (Courneya et al., 2015). Finally, engaging in an adequate level of physical activity may even be associated with a reduced risk of recurrence in certain cancers, such as colon cancer (Meyerhardt et al., 2006). Therefore, physical activity improves quality of life, encourages the adoption of healthy behaviours and lifestyles, facilitates the recovery of autonomy, promotes socialization, and contributes to reducing anxiety and depression. In fact, the World Health Organization (WHO) guidelines recommend that adults engage in at least 150–300 minutes of moderate-intensity aerobic exercise or 75–150 minutes of vigorous-intensity exercise per week in order to maintain overall health and reduce the risk of noncommunicable diseases (WHO, 2025b).

Evidence from non-oncological orthopedic surgery suggests that higher levels of preoperative physical activity are associated with faster postoperative functional recovery. Engaging in physical activity before surgery can enhance muscle strength, reduce pain, and improve overall physical function, leading to a more rapid postoperative recovery after knee and hip arthroplasty surgery (Vasta et al., 2020). Postoperative physical activity has been shown to accelerate functional recovery, enhance mobility and strength, reduce pain and complications, and improve patient satisfaction in orthopaedic surgery patients, while in cancer patients it can also increase cardiorespiratory capacity, walking distance, quality of life, and reduce fatigue (Beyer et al., 2025; Cao et al., 2025).

Despite evidence supporting the benefits of physical activity, most studies in oncology patients have focused on exercise performed after diagnosis and during treatment. Less is known about the role of preoperative physical activity in orthopedic oncology patients and its potential impact on post-surgical recovery time and outcomes, as current literature has received limited attention regarding whether an active lifestyle prior to diagnosis and surgery could facilitate a faster and more effective recovery. Therefore, the aim of this experimental study is to investigate whether a physically active lifestyle practiced prior to oncologic surgery may serve as a predictive factor for a faster and more effective motor recovery in patients with musculoskeletal tumors. The study aims to determine whether pre-diagnostic physical activity can positively influence the timing and quality of postoperative recovery.

5.2 Methods

Patients

This study followed an observational, cross-sectional design. The study population consisted of 20 patients (13 females, 7 males; mean age 50.1 ± 15.7). Inclusion criteria were: age ≥16 years, histologically confirmed diagnosis of a bone or soft tissue tumor located in the lower limb or lower back, and independent ambulation without the use of assistive devices. All patients had already been scheduled for surgical intervention involving either bone resection or excision of soft tissue lesions and were assessed once during their preoperative hospital admission. Written informed consent was obtained from all participants.

The study protocol received approval from the Central Ethics Committee of the Istituto di Ricovero e Cura a Carattere Scientifico (I.R.C.C.S.) Lazio – I.R.C.C.S. I.F.O. (Clinical Trial Register No. 1704/22).

Experimental Protocol

All assessments were conducted at the time of hospital admission at the IFO IRE Regina Elena Institute in Rome, with follow-up assesments performed six months after the intervention. Participants were equipped with 6 wearable inertial sensors (OPAL, APDM Inc.; sampling frequency 128 Hz) positioned on the head, sternum, lower back, upper and lower limbs, and hands to enable full-body motion capture. Participants completed the instrumented Timed Up and Go (iTUG) test and the static balance assessment in a randomized order to minimize potential order effects. The iTUG involved standing up from

a standard-height chair, walking three meters, turning around, returning to the chair, and sitting down, while the static balance assessment required participants to stand quietly in a natural stance for 30 seconds, focusing on a fixed point at eye level. The two-minute walking test (2MWT) was always performed last due to its higher physical demand, which could have induced fatigue and influenced performance on the preceding tasks. Pain experienced during walking was evaluated using a Numeric Rating Scale (NRS) from 0 (no pain) to 10 (worst imaginable pain) to report the level of pain experienced during walking, providing a subjective evaluation of discomfort. To determine PA levels, information on the duration of each training session, the weekly frequency, and the type of the performed physical activity and were collected.

Data collection and statistical analysis

Spatiotemporal gait parameters, iTUG performance, trunk kinematics, turning metrics, and postural sway measures were analysed using the Moveo Explorer software with built-in algorithms (Fang et al., 2018; APDM, n.d.; Monaghan et al., 2024; Morris et al., 2019). For each motor task, specific parameters were extracted. Gait parameters included gait speed (m/s) and cadence (steps/min), calculated as the mean of both limbs, as well as stance (% Gait Cycle Time, GCT), swing (%GCT), double support (%GCT), and stride length (m) for both the tumor-affected limb (T) and the contralateral healthy limb (H). This limb-specific approach allowed a more detailed characterization of compensatory strategies and functional impairments potentially associated with the tumor, which could be overlooked when only global gait metrics are considered. For the iTUG test, extracted metrics included total duration (s), turn duration (s), sit-to-stand and stand-to-sit durations (s), and the corresponding trunk lean angles (°). Postural control was assessed through sway area (m^2/s^4) and Root Mean Square (RMS) measures in the overall, coronal, and sagittal planes (m^2/s^4). Raw motor data were processed using preconfigured algorithms provided by the Moveo Explorer® software. During a patient interview, specific questions were used to capture the frequency of exercise sessions (sessions per week), the duration of each session (minutes), and the type of activities performed in order to estimate exercise intensity (e.g. slow or fast walking, cycling, etc). The data obtained were subsequently processed according to the criteria established by the PASSI (Progressi delle Aziende Sanitarie per la Salute in Italia) surveillance system (Istituto Superiore di Sanità [ISS], n.d., Indicatori Passi: Attività fisica), which classifies adults into three profiles: active, defined as those engaging in at least 150 minutes of moderate-intensity physical activity per week or at least 75 minutes of vigorous

activity; partially active, referring to individuals performing less than 150 minutes per week but with some regularity; and sedentary, comprising those who do not engage in regular physical activity or exercise only occasionally. For the purposes of analysis, participants were further grouped into two main categories: the active group, including both “active” and “partially active” individuals, and the sedentary group, which included only participants classified as sedentary.

For within-group comparisons, variables with a normal distribution were analyzed using the paired-samples t-test to compare pre- and post-intervention data, whereas for non-normally distributed variables, the Wilcoxon signed-rank test was applied. Between-group comparisons, aimed at detecting significant differences between active and sedentary participants, were conducted using the independent-samples t-test for normally distributed variables and the Mann-Whitney U test for variables not normally distributed.

5.3 Results

Based on the analysis of data collected through the preoperative questionnaire, it was possible to estimate the level of physical activity performed by each participant prior to cancer diagnosis. According to the classification criteria, 8 participants were categorized as active (AP), while the remaining 12 were classified as sedentary (SP). Patients’ characteristics are reported in Table 6. Significant results are shown in Figure 4 and Table 7.

Table 6 *– Clinical, oncological and behavioral characteristics of the patients included in the study*

Groups	Age	Gender	Type of Tumor	Tumor Location	Tumor Volume (cm^3)	Surgery	Chemio/Radio Pre-Post intervention	Pain Level (NRS) Pre-Post intervention	Occupation	PA Frequency times/week	PA Sessions Duration (min)	Type of Activity
AP (8)												
1	48	F	Bone	Femur	1356,48	Resection and endoprosthetic reconstruction	No	10 - 5	Financial Assistant	1-2	30-60	Walking
2	17	F	Bone	Knee	11663,53	Exostosis excision	No	7 - 1	Student	1-2	30-60	Other
3	62	F	Soft Tissue	Thigh	572233,60	Wide excision	No	-	Office sitting job	3-4	30-60	Walking, cycling, light exercise, swimming
4	69	M	Soft Tissue	Thigh	399907,26	Wide excision	No	0 - 0	Retired	1-2	15-30	Walking
5	22	M	Soft Tissue	Abductor	24793,44	Wide excision	Yes (Pre)	2 - 0	-	3-4	30-60	Walking, light exercise, weight training
6	40	F	Soft Tissue	Ankle	9158,33	Wide excision	No	6 - 7	-	1-2	30-60	Walking
7	66	F	Soft Tissue	Glute	217706,667	Wide excision	No	0 - 0	Retired	> 4	30-60	Walking
8	60	M	Soft Tissue	Psoas	128216,667	Wide excision	No	0 -1	-	3-4	> 60	Walking
SP (12)												
9	50	F	Bone	Sacrum	20582,7	Bone resection	No	5 -7	Nurse	<1	30-60	Walking
10	65	M	Bone	Iliac Crest	50370,8333	Bone excision	No	7 -0	Retired	None		
11	48	M	Bone	Knee	4186,66667	Curettage and bone grafting	No	8 - 8	Office sitting job	None		
12	41	F	Bone	Pelvis	155744,00	Wide resection and bone grrafting	Yes (Pre)	0 - 5	Housewife	None		
13	60	F	Bone	Pelvis	421796,20	Resection	Yes (Pre-Post)	5 - 3	School Assistant	None		
14	21	F	Bone	Tibia	36332,94	Bone excision	No	9 - 5	-	<1	15-30	
15	69	F	Soft Tissue	Thigh	126922,99	Wide excision	No	0 - 0	-	<1	30-60	Light exercise
16	45	M	Soft Tissue	Thigh	628,00	Wide excision	Yes (Pre)	0 - 0	Electrician	None		
17	52	F	Soft Tissue	Thigh	784429,57	Wide excision	No	0 - 5	Housekeeper	None		
18	63	F	Soft Tissue	Popliteal Fossa	5878,08	Wide excision	Yes (Pre)	0 - 0	Retired	None		
19	54	M	Soft Tissue	Thigh	30497,25	Wide excision	No	1 - 0	Nurse	>4	< 15	Walking, cycling, mobility exercise
20	50	F	Soft Tissue	Thigh	114212,27	Wide excision	No	0 - 0	-	None		

Within-group Analysis

In the active group, pre- to post-intervention comparisons revealed no statistically significant differences for any of the variables analyzed. For the iTUG test, neither the walking duration ($p = 0.988$), turn duration ($p = 0.346$), nor turn velocity ($p = 0.906$) showed significant changes. Sit-to-stand duration ($p = 0.360$) and lean angle ($p = 0.483$), as well as stand-to-sit duration ($p = 0.899$) and lean angle ($p = 0.381$), did not differ between pre- and post-assessments. Similarly, sway area ($p = 0.674$) and RMS sway ($p = 0.674$) in the Sway test did not exhibit significant changes. In the 2MWT, no significant pre-post differences were observed for cadence ($p = 0.854$), gait speed ($p = 0.568$), stance phase for the healthy ($p = 0.159$) and operated limb ($p = 0.372$), swing phase for the healthy ($p = 0.159$) and operated limb ($p = 0.372$), or stride length for the healthy ($p = 0.400$) and operated limb ($p = 0.511$).

Within the sedentary group, pre- to post-intervention comparisons similarly showed no significant differences for most parameters. For the iTUG test, walking duration ($p = 0.224$), turn duration ($p = 0.930$), turn velocity ($p = 0.595$), sit-to-stand duration ($p = 0.102$), sit-to-stand lean angle ($p = 0.218$), stand-to-sit duration ($p = 0.415$), and stand-to-sit lean angle ($p = 0.445$) did not change significantly. No significant changes were observed in the Sway test, including sway area ($p = 0.937$) and RMS sway ($p = 0.126$).

However, in the 2MWT, some differences emerged. Specifically, swing phase of the healthy limb showed a significant change ($p = 0.020$), as did stride length of the operated limb ($p = 0.026$). Other parameters, including cadence ($p = 0.213$), gait speed ($p = 0.084$), stance phase ($p = 0.059$), swing phase of the operated limb ($p = 0.981$), and stride length of the healthy limb ($p = 0.068$), did not reach statistical significance.

Between-group Analysis

Comparisons between the active and sedentary groups at both preoperative and postoperative assessments revealed several significant differences, suggesting a more favorable functional recovery in patients who had engaged in regular physical activity prior to surgery.

For the iTUG test, most parameters did not differ significantly between the two groups at either time point. Specifically, total walking duration (Pre: $p = 0.295$; Post: $p = 0.177$), sit-to-stand duration (Pre: $p = 0.423$; Post: $p = 0.856$) and lean angle (Pre: $p = 0.275$; Post: $p = 0.931$), as well as stand-to-sit duration (Pre: $p = 0.290$; Post: $p = 0.300$) and lean angle (Pre: $p = 0.130$; Post: $p = 0.934$), did not show significant differences. However, variables related to the turning phase revealed notable differences: turn duration was significantly shorter in the active group postoperatively ($p = 0.024$), and turn velocity was highly significantly greater ($p < 0.001$), indicating improved motor control during turning in the active group.

For the Sway test, no postural parameters differed significantly between groups. Sway area (Pre: $p = 0.440$; Post: $p = 0.143$) and RMS sway (Pre: $p = 0.396$; Post: $p = 0.932$) showed no significant changes.

In the 2MWT, most parameters did not differ significantly between groups at either assessment. No significant differences were observed for cadence (Pre: $p = 0.838$; Post: $p = 0.733$), gait speed (Pre: $p = 0.299$; Post: $p = 0.363$), stance phase of the healthy (Pre: $p = 0.307$; Post: $p = 0.563$) or operated limb (Pre: $p = 0.407$; Post: $p = 0.571$), or swing phase of the healthy (Pre: $p = 0.307$; Post: $p = 0.375$) or operated limb (Pre: $p = 0.407$; Post: $p = 0.571$).

Notably, stride length showed significant differences postoperatively, with both the healthy ($p = 0.037$) and operated limb ($p = 0.045$) exhibiting greater step length in the active group compared to the sedentary group. These differences were not present preoperatively ($p = 0.334$ and $p = 0.112$, respectively), supporting a beneficial effect of preoperative physical activity on postoperative gait performance.

Figure 4 *– Solid lines represent active patients (AP), while dashed lines represent sedentary patients (SP). An improvement in performance is indicated by a positive slope (upward), whereas a decline is indicated by a negative slope (downward). § Represents within-group pre-post significant differences. * Represents between-group significant difference.*

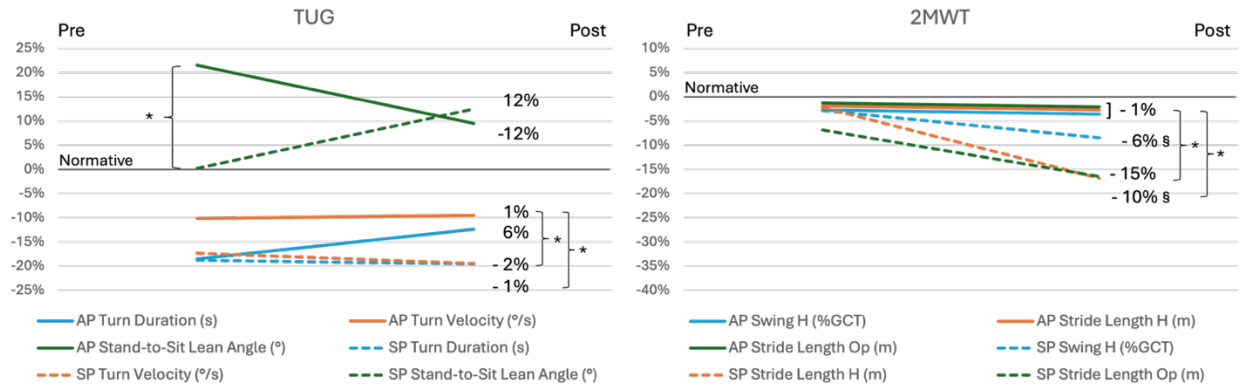

Table 7 *– Table reports group mean and standard deviation (SD) of each parameter for each proposed motor task. * Between-groups significant difference; § Within-group significant difference.*

	AP				**SP**			
	Pre		*6 months*		*Pre*		*6 months*	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
2MWT								
Gait Speed (m/s)	1.03	0.18	1.01	0.16	0.94	0.14	0.83	0.23
Cadence (stesp/mn)	110.04	9.90	109.59	9.28	108.21	10.77	104.79	10.69
Stance Op (%GCT)	60.45	1.50	60.78	1.91	60.80	2.15	60.81	1.80
Stance H (%GCT)	60.74	1.32	61.09	1.36	60.78	1.87	62.89	5.06
Swing Op (%GCT)	39.55	1.50	39.23	1.91	39.20	2.15	39.19	1.80
Swinge H (%GCT)	39.26	1.32	38.91	1.36	39.23§	1.87	36.94§	4.99
Stride Length Op (m)	1.11	0.12	1.10*	0.10	1.05§	0.08	0.94§*	0.19
Stride Length H (m)	1.10	0.11	1.10*	0.09	1.10	0.25	0.94*	0.19
TUG								
Duration (s)	12.06	2.64	12.08	1.94	12.46	1.87	14.23	3.91
Turn Duration (s)	2.45	0.34	2.33*	0.17	2.46	0.36	2.47*	0.53
Turn Velocity ()	161.38	25.38	162.50*	13.18	148.50	29.09	144.70*	35.08
SiSt Duration (s)	0.99	0.11	1.06	0.18	1.08	0.15	0.98	0.18
SiSt Lean Angle (°)	21.98	9.46	25.06	6.86	23.44	5.84	20.80	6.62
STSi Duration (s)	0.82	0.18	0.83	0.17	0.97	0.29	1.07	0.30
STSi Lean Angle (°)	18.21*	5.69	21.00	7.27	23.27*	10.05	20.32	8.89
Sway								
Sway Area	0.01	0.01	0.01	0.02	0.02	0.01	0.02	0.01

RMS Sway	0.05	0.01	0.05	0.03	0.06	0.02	0.05	0.02
RMS Coronal	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.01
RMS Sagittal	0.05	0.01	0.05	0.02	0.06	0.02	0.05	0.02
NRS	3.57	4.08	2.00	2.83	2.92	3.60	2.75	3.11

5.4 Discussion

The aim of this study was to analyze the impact of preoperative physical activity on the functional parameters of patients with musculoskeletal tumors who underwent surgery. The division of participants into two groups, “active” and “sedentary,” allowed for the observation of different trends in the results of functional tests.

Intra-group analysis did not reveal any statistically significant changes in active patients, suggesting relative stability in motor performance between pre- and post-surgery. This could be interpreted as a protective effect of physical activity: active subjects, starting from a higher functional level, would tend to maintain their motor skills more easily, despite surgery. Therefore, the absence of decline may be a positive sign of physical resilience, which is consistent with evidence showing that preoperative exercise ("prehabilitation") can improve postoperative recovery and maintain functional capacity (Minnella et al., 2018; Santa Mina et al., 2014; Silver, 2015). This finding is somewhat in contrast with the results reported in previous reviews and meta-analyses, which either reported no effect of prehabilitation (Poortinga et al., 2014) or detected an improvement, albeit not significant (López-González et al., 2025). However, it should be noted that the prehabilitation interventions in the studies considered last for a few weeks. It has been demonstrated that for an intervention to be effective, a minimum of 8 weeks in special populations (Jan et al., 2008), or 12 weeks in elderly (Karelis et al., 2015) is required. Furthermore, the efficacy of the intervention is not always ascertained through a test comparing baseline and after prehab treatment functional abilities, prior to the intervention. Moreover, in some cases, the effects are evaluated solely through the administration of questionnaires (Poortinga et al., 2014). The patients in the present study, instead, engage in physical activity as a habitual and lifestyle component. Consequently, it can be hypothesized that an active lifestyle exerts a more significant influence than a timed prehabilitation training protocol.

In the sedentary group, on the other hand, there was a significant variation in the swing phase of the healthy limb and in the stride length of the operated limb in the 2MWT. These changes could reflect post-surgical motor compensation coherently with previous meta-analysis on this population (Filis et al., 2022). Previous studies have shown that physical inactivity increase predisposition to motor deterioration and impairs compensatory mechanisms after surgery or injury (Booth et al., 2012).

The *intergroup analysis* offered relevant insights. In particular, in the iTUG test, turn velocity and turn duration showed significant differences 6 months post intervention, with better performance in active subjects. These results are particularly interesting as the rotation phases involve greater demands on coordination, postural control, and body weight transfer ability, and movement planning systems (Belluscio et al., 2021; Chia Bejarano et al., 2017), and the fact that active subjects maintained or improved these parameters suggests more effective movement control and better post-operative neuromuscular adaptation. These findings align with earlier studies, underscoring the importance of the turning phase as both demanding and informative. This supports the view that phase-specific analyses are more effective in capturing functional limitations (Mangano et al., 2020). These data are consistent with the findings of previous studies that have indicated that regular physical activity contributes to improvements in strength, endurance, coordination, balance, and the quality of motor and neuromuscular control. (Lindström et al., 2009).
Prior to undergoing surgery, patients who were physically active demonstrated a reduced stand-to-sit lean angle in comparison to sedentary individuals. This finding indicates that physically active patients may employ a more efficient and controlled movement strategy. This observation is consistent with prior research indicating that regular physical activity enhances neuromuscular coordination, strength, and postural control. Consequently, this results in a reduction of compensatory trunk flexion and an improvement in the smoothness of transitional movements (Lin and Lee, 2022).

In the 2MWT, the absence of significant differences in the preoperative phase and their appearance after surgery could suggest that physical activity facilitated a faster and more complete recovery, reflected in a wider and more fluid gait. In fact, a reduction in stride length in the postoperative phase, both for the healthy limb and the operated limb, as observed in sedentary patients, is still consistent with previous literature (Filis et al., 2022), which report this as a post-surgical functional modification.

The lack of differences in postural parameters (Sway Area and RMS Sway) is consistent with previous findings (de Visser et al., 2001), when performing an eyes-opened upright standing task. Postural control is a dynamic and adaptive process that relies on the integration of somatosensory, visual, and vestibular information to maintain postural orientation, defined as the alignment of the body with respect to gravity, the supporting surface, and visual cues. And the maintenance of postural equilibrium, is the stabilizing of the center of mass against external or internal disturbances (Horak, 2006). Consequently, the present findings may indicate that, in the absence of specific sensory challenges, the coordinated interaction among these sensory systems is sufficient to maintain postural stability under eyes-open and firm-surface conditions, even in the presence of a localized biomechanical alteration (de Visser et al., 2001; Karasimav et al., 2024). Concurrently, the extant evidence suggests that more challenging tasks are required. This assertion is supported by the findings of de Visser et al. (2001).

Importantly, the active and sedentary groups showed a similar clinical heterogeneity in terms of tumor location, volume, and extent of surgical intervention. Therefore the overall variability of the cohort may have partially limited the detection of stronger or more consistent effects on functional outcomes, related to preoperative physical activity.

Overall, the results of this study suggest that physical activity performed in the preoperative phase may play a positive role in supporting motor function and promoting postoperative recovery in musculoskeletal cancer patients. More specifically, these effects seem to be more evident in complex motor tasks, which require the fine integration of multiple motor and neuromuscular components. In particular, physical activity appears to have a protective effect on motor skills, helping to preserve functionality in tasks such as rotation or stride length, which require fine integration between neuromuscular control, balance, and coordination.

The results obtained indicate that physically active patients, while not showing significant improvements within their own group, were able to maintain a more stable functional level than sedentary patients, for whom variations emerged that could reflect a lower capacity for post-operative adaptation. Furthermore, the inter-group differences observed in the TUG test and the 2-Minute Walk Test suggest a more efficient motor recovery in active subjects.

However, these results should be considered with caution due to the limited number of participants, and the high variability of this population which might influence the statistical

results. Further studies with larger samples will be necessary to confirm these results and to better understand the mechanisms through which preoperative physical activity can influence the postoperative course.

5.5 Conclusions

The evidence gathered in this pilot study, although preliminary and limited by the small sample size, suggests that an active lifestyle in the preoperative phase can positively influence the postoperative course in cancer patients with musculoskeletal tumors.

These data reinforce the idea that physical activity should not only be considered part of post-operative rehabilitation, but also an integral component of pre-operative preparation, with potential benefits in terms of functional outcomes and quality of life.

However, further studies on larger samples and with prolonged follow-up will be necessary to further validate these results and investigate the mechanisms through which physical activity affects post-surgical recovery processes.

In a healthcare context increasingly oriented towards the personalization of therapeutic pathways and the overall improvement of the patient's quality of life, the introduction of structured and timely motor interventions in the preoperative phase therefore appears to be a promising prospect, capable of enhancing the interdisciplinarity between oncology, rehabilitation, and motor sciences. Promoting a model of care focused not only on the disease but on the person as a whole also means recognizing and valuing movement as a fundamental therapeutic resource throughout the continuum of care.

Chapter 6 – Integrating Laboratory and Real-Life Assessments in Proximal Tibial Replacement Patients: An Overview of the STanmore OutcoMes Project (STOMP)

This chapter summarizes the observations made during the research period at the Royal National Orthopaedic Hospital (RNOH), London, as part of the present PhD project. This work was conducted as a sub-study of the ongoing clinical research program, the Stanmore Tumor OutcoMes Project (STOMP), coordinated by the RNOH.

For the present sub-study, we selected a specific cohort of patients who underwent proximal tibial replacement (PTR) following resection of bone tumors. This subgroup was chosen both for practical reasons, availability of eligible patients at the hospital, and for scientific rationale: focusing on a homogeneous patient group allows a more detailed and controlled analysis of postoperative functional outcomes, compensatory strategies, and multidimensional patient experience. The PTR procedure represents a complex surgical intervention with well-defined biomechanical implications, making it an ideal model to explore objective gait, balance, and functional performance using wearable sensors and standardized assessment tools.

The Stanmore Tumor Outcomes Project (STOMP) is a long-term, multidisciplinary research initiative at the Royal National Orthopaedic Hospital. It aims to comprehensively evaluate recovery trajectories following surgical treatment for musculoskeletal tumors, addressing functional, mobility, and quality-of-life outcomes alongside traditional oncological measures. STOMP integrates standardized clinical and patient-reported outcome measures with objective assessments, including wearable sensors, to capture detailed information on postoperative function and real-world mobility. By linking tumor characteristics, surgical variables, and rehabilitation trajectories, STOMP seeks to identify predictors of recovery and support evidence-based, personalized care for patients undergoing complex orthopedic tumor surgery.

(Adapted from publicly available information on the Stanmore Tumour OutcoMes Project, Royal National Orthopaedic Hospital NHS Trust, UK)

6.1 Gait, Balance, and Physical Activity after Proximal Tibial Replacement for Musculoskeletal Tumours: A Narrative Review

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6.1.1 Introduction

Proximal tibial replacement (PTR) is a limb-salvage surgical option commonly employed in the treatment of bone tumors involving the proximal tibia. Proximal tibial replacement consists of a proximal tibial bone resection and implantation of a modular metallic endoprosthesis that matches the length of the resected bone. One of the most critical steps of the procedure, however, is reconstruction of the extensor mechanism, which is often compromised by the proximal tibial resection. The patellar tendon is reattached to the prosthesis using synthetic mesh, an autograft (e.g., fascia lata), or an allograft, which are sutured to fixation holes or porous coatings on the anterior surface of the prosthesis (Pilge et al., 2015). The goal is to restore continuity between the quadriceps tendon, patella, and tibial prosthesis to enable active knee extension. To enhance soft-tissue coverage and reduce the risk of wound complications, a medial gastrocnemius muscle flap is often mobilized and rotated anteriorly to cover the implant and reconstructed tendon.

While advances in oncological treatment and surgical techniques have improved survival rates (Mavrogenis et al., 2013), optimizing postoperative functional outcomes remains a key concern in this patient population. Gait, physical activity (PA), and balance are crucial domains that contribute to overall quality of life, autonomy, and long-term musculoskeletal health in patients undergoing limb salvage procedures.

Despite this, current literature often groups PTR patients with those receiving distal femoral replacements (DFR), without accounting for the distinct biomechanical and functional challenges associated with PTR. The anatomical and muscular disruptions following PTR, including quadriceps mechanism reconstruction and extensor lag, suggest a unique postoperative recovery profile that may not be adequately reflected when analyzed in mixed cohorts (Kim et al., 2021a).

To date, comprehensive overview of gait, physical activity, and balance data specific to PTR is lacking, as PTR is frequently grouped with distal femoral replacement DFR despite their distinct biomechanical characteristics, as highlighted in recent studies. This represents a gap

in the literature, limiting clinicians' ability to obtain a comprehensive overview of the patient's functional status across multiple domains, providing objective data to guide the planning of targeted rehabilitation interventions and offering valuable information to orthopedic surgeons regarding the outcomes of surgical treatments in this specific patient population.

Therefore, the aim is to summarize the current evidence on objective assessments of gait, physical activity, and balance in proximal tibial replacement patients, providing a comprehensive, multidimensional functional analysis of oncology patients with a PTR and exploring potential interrelationships among these functional domains.

6.1.2 Methods

Literature Search Strategy

A comprehensive literature search was performed using the electronic databases MEDLINE and EMBASE, including studies published up to April 2025. A core search strategy combining terms related to bone sarcomas, proximal tibial replacement (PTR), and the relevant functional outcomes was constructed using Boolean operators (AND). This base string was adapted for each of the three domains of interest: gait, physical activity levels, and balance.

Study Selection and Eligibility

After deduplication, titles and abstracts were screened for relevance. Full texts were retrieved and assessed for eligibility.

Inclusion Criteria

Studies were included if they met the following criteria:

- Investigated patients who had undergone proximal tibial replacement for bone tumors;
- Reported data on at least one of the following domains: gait, physical activity levels, or balance;
- Employed objective measurement tools (e.g., motion analysis systems, wearable sensors, force platforms, or accelerometery);
- Studies with mixed cohorts (e.g., PTR and distal femoral replacement) were included only if data specific to the PTR group could be clearly identified and extracted.

Exclusion Criteria

- Conference abstracts or proceedings
- Articles not written in English
- Articles not available in full text
- Review articles
- Studies on upper limb or distal tibial replacements
- Studies using only clinical tests (e.g., TUG, TUDS) without detailed biomechanical or outcome-specific analysis
- Studies with mixed cohorts in which outcomes could not be distinguished and isolated for PTR patients were excluded.

Adaptations to Inclusion Criteria

Due to the limited number of studies focused exclusively on PTR patients in the domain of balance, mixed cohorts (e.g., PTR and distal femoral replacement) were included if the results were clearly described and clinically relevant to PTR patients

Data Extraction

Key data were extracted and organized in a structured table, including:

- Author(s) and year
- Study title and objective
- Number and characteristics of patients
- Tumor location
- Type of surgical procedure/implant
- Time from surgery to assessment
- Measurement tools and tasks performed
- Outcome parameters analysed
- Key results and authors' conclusions

Studies were grouped under the relevant domain(s) based on their primary focus.

6.1.3 Results

A total of 955 articles were identified through the literature search. Following screening and eligibility assessment based on the inclusion and exclusion criteria, 10 studies were included in the review. The identification process is showed in Figure 5.

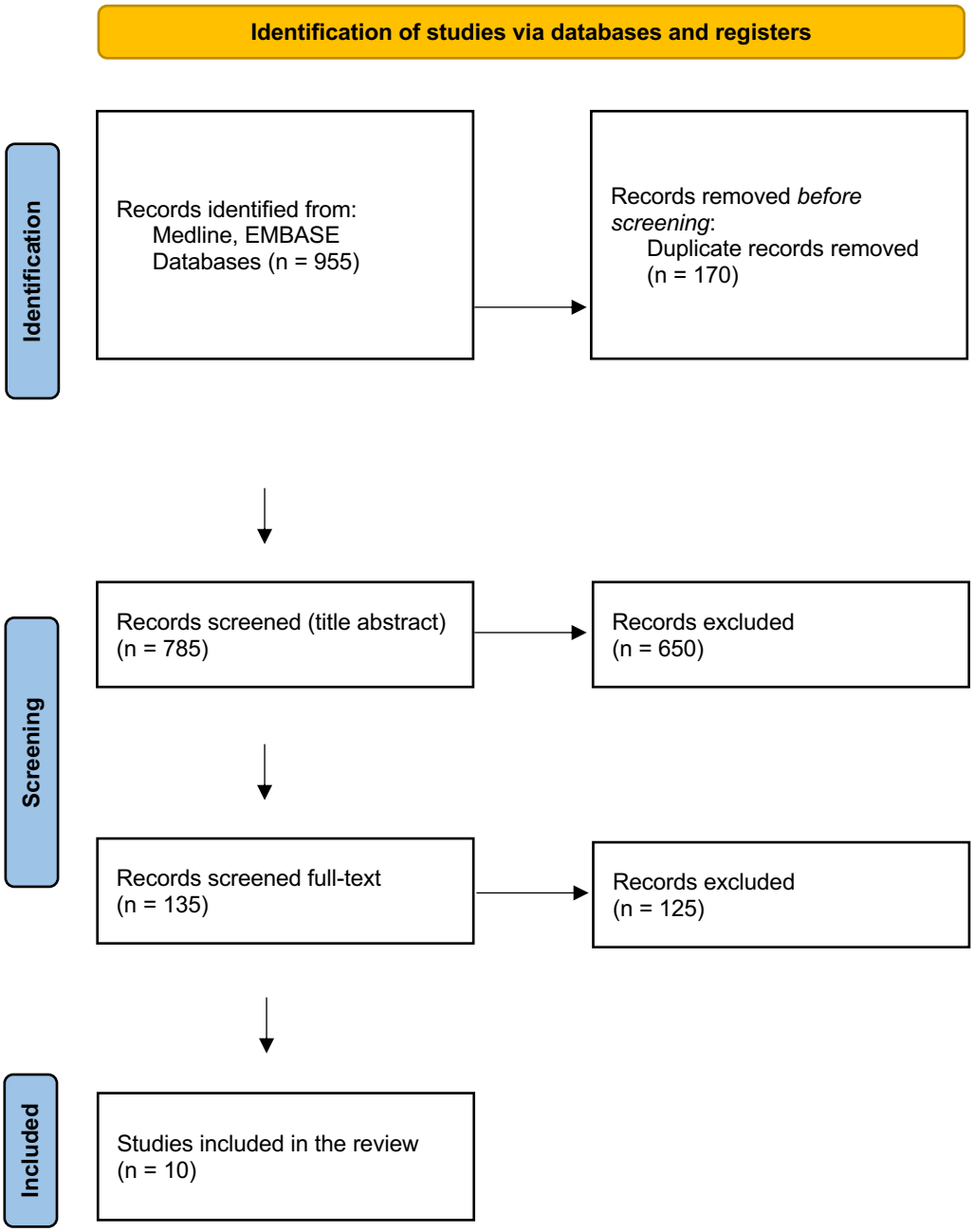

Figure 5 *– PRISMA-style flow chart of the literature screening process.*

The studies ranged from 1997 to 2024, with an increase in publications on this topic observed since 2015 (Figure 6).
The included studies were categorized according to the three main domains of investigation: gait, physical activity levels, and balance.

Five studies focused on gait analysis, two on physical activity levels assessment, two on balance and one focused on both gait and PA levels assessment. The distribution of studies across these categories is illustrated in Figure 7. Main results are summarized in Table 8.

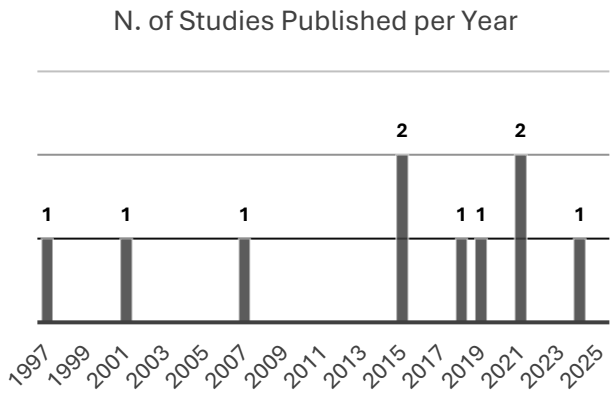

Figure 6 *– Distribution of the studies included in the review by year of publication.*

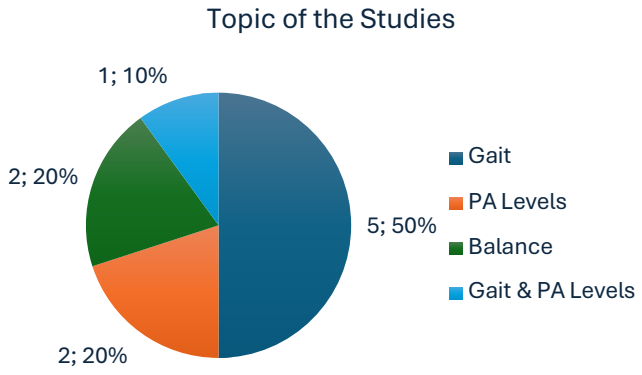

Figure 7 *– Pie chart showing the number of paper and percentage of articles included in the review per topic category*

Table 8 *– Objective functional assessment overview*

Author & Year	Domain	Sample/tumor location	Time from Intervention	Sample (PTR vs. CG vs. DFR)	Setting	Task	Correlations/ Predictions	Main conclusions
Morri et al., 2018	Balance	Distal femur (12) Proximal tibia (3)	12 months	PTR&DFR	Manual goniometer MRC scale Stabilometric platform (LorAn Engineering Srl – Sistema EPS-R1) Questionnaires: MSTS, TESS	Balance: 10s standing, eyes opened and eyes closed Gait performance tests: Walk 10m - speed 6MWT - resistance TUG - mobility	Balance correlated with Gait speed, gait resistance and functional ability (TUG)	In patients one year post-knee endoprosthetic reconstruction for bone tumors, balance control was significantly correlated with all gait performance tests. Additionally, age, chemotherapy duration, and knee extensor strength showed correlations, suggesting balance-focused rehabilitation addressing the entire sensory and motor system is crucial
Morri et al., 2019	Balance	Distal femur (15) Proximal tibia (7)	12 months	PTR&DFR	Manual goniometer MRC scale Questionnaires: MSTS, TESS Stabilometric platform (LorAn Engineering Srl – Sistema EPS-R1)	Balance: de Visser et al. method Gait performance tests: Walk 10m 6MWT TUG	No	A rehabilitation protocol incorporating game balance exercises significantly improved walking speed and postural control (reduced speed of center mass) in patients one-year post-knee resection and modular prosthetic replacement for primary bone tumors. This indicates that such interventions are effective for enhancing motor performance and postural stability in this patient group.
Sugiura et al., 2001	PA Levels	Bone Tumors: Distal femur (9) Proximal tibia (5) Proximal femur (3) Proximal fibula (2) Femoral shaft (1)	4.3 ± 2.1 years		Pedometer (Omron Health Counter HJ-5, Japan, accuracy 95%) Questionnaires: ADL MSTS	Patients used the pedometer for 2 weeks	correlations between the number of steps and ADL score, Enneking score, MMT, and active range of motion in the lower limbs	Patients who underwent limb salvage for lower limb tumors averaged 69.8% of control group's daily steps, with bone tumor patients showing significantly lower activity and functional scores than soft-tissue tumor patients. The study concluded that the number of steps (pedometer-measured) and the ADL score are useful functional evaluations, showing significant correlations with the Enneking score
Bernthal et al., 2015	PA Levels	Bone sarcoma: Proximal femur (7) Distal femur (8) Proximal tibia (7)	13.2 years (range, 2.5–28.2 years)		MSTS Portable breath-by-breath pulmonary gas exchange unit (K4 b2; Cosmed, Rome, Italy) 58-m oval pathway Isokinetic dynamometer (System 4 Pro; Biodex, Shirley, NY, USA) at 60°/s Stepwatch Activity Monitor (Orthocare Innovations, Oklahoma City, OK, USA)	Overground walking data collected at a self-selected speed for a minimum of 6 minutes and continued until steady-state had been maintained for at least 4 minutes. Knee extensors and flexors strength Stepwatch above the ankle of one limb for 1 week	No	Patients with lower extremity endoprosthetic reconstructions after tumor resection demonstrated efficient gait (comparable oxygen consumption and walking speed to controls) and were active at home and in the community at a mean of 13.2 years post-surgery. While maintaining similar activity levels, patients with proximal tibia replacements specifically exhibited reduced knee extension and flexion strength compared to other reconstruction groups
Gundle et al., 2017	PA Levels (Vlidation)	Treated lower extremity primary bone tumor (25)	49 (±62) weeks	PTR Validation	Activity monitor (FitBit One; FitBit, San Francisco, CA) TESS 36 version 2 (SF36)	Wear daily until the battery died	Average daily steps and SF6D Average daily steps and SF36 PCS Time from surgery and average daily steps Time from surgery and SF6D SF36 PCS and TESS	A made-for-consumer activity monitor (FitBit One) was validated as a tool to assess real-world physical activity in adolescents and young adults after lower extremity limb salvage. The study found that average daily steps correlated moderately with physical health outcomes (SF36 PCS, SF6D) and strongly with the time elapsed since surgery

Fowler et al., 2021	Gait & PA Levels	Bone Tumor: Proximal Tibia (9)	14,1 (11,2) years	PTR	- MMT (Manual Muscle Testing) - MSTS - Isokinetic dynamometer (System 4 Pro; Biodex, Shirley, NY, USA) - Eagle 8-camera system (Motion Analysis Corporation, Santa Rosa, CA)(modified Helen Hayes marker set) - 2 Kistler force plates (Kistler Instrumen-tation Corporation, Amherst, NY) Overground walking - The StepWatch TM Activity Monitor (Modus Health LLC, Washing ton, DC) - Short form 36 version 1 (SF-36)	Participants walked barefoot at preferred and fast (as fast as possible without running) speeds. StopWatch device worn above one ankle, wear the monitor three to five weekdays and two weekend days.	No	This study revealed that patients undergoing proximal tibial tumor resection and endoprosthetic reconstruction (PTR) exhibit significant gait abnormalities characterized by knee extensor and ankle plantar flexor weakness, abnormal knee kinematics, and reduced single limb support time. Despite these identified deficits, patients' walking speed and health-related quality of life (SF-36 scores) were found to be relatively normal, though they showed a higher percentage of low-frequency strides during community walking
Almeida et al., 2024	Gait	Bone Tumor: Distal Femur (12) Proximal Tibia (5)	39 months	PTR vs. DFR vs. CG	8-camera infrared emission system (Qualisys, Oqus 300) 2 Bertec forceplates (FP 4060–08) Reflective markers - Helen Heyes (Kabada) protocol 6m Runway (habitual speed)	Walked at habitual speed. Each patient walked at least five times along the entire 6-m runway	No	This study revealed that patients with knee endoprosthesis after either distal femur (DFR) or proximal tibia (PTR) resection exhibit significant gait alterations compared to healthy controls, particularly in spatiotemporal parameters. Although major kinematic and kinetic differences between DFR and PTR groups were not consistently found to be statistically significant, PTR patients notably tend to maintain knee extension throughout the stance phase
Kim et al., 2021	Gait	Bone Tumor: Distal femur (7) Proxilam Tibia (9)	5.3 years	PTR vs. DFR	MSTS eight-camera system (Motion Analysis Corp., Santa Rosa, CA, USA; 120 Hz) 2 Forceplates (9260AA6; Kistler Instrumente AG, Winterthur, Switzerland) 7m walkway Markers: Helen Hayes marker set	walk barefoot on a 7 m walkway >3 times Collected and averaged data for >3 successful trials	No	This study revealed that gait patterns after knee endoprosthesis significantly differ based on tumor location (distal femur vs. proximal tibia). These variations, affecting knee, hip, and ankle parameters, highlight the necessity for distinct, location-specific rehabilitation strategies
Pilge et al., 2015	Gait	Bone Tumor: Proximal Tibia (9)	11.6 years		Isobex machine Blackburne-Peel-index (BPI) Treadmill video analyses, kinematic and force data	Isokinetic measurement Walk - treadmill	No	This study found that the patellar-loop technique for extensor mechanism reconstruction after proximal tibia tumor replacement provides good biomechanical and functional results. Patients demonstrate a gait pattern close to normal, although with some knee stiffness and reduced but sufficient extensor strength
Colangeli et al., 2007	Gait	Bone Tumor: Proximal Tibia (18) [TKA (10), AL (8)]	TKA: 63 months AL: 37 months	TKA vs. Osteochon dral allograft	ELITE stereophotogra mmetric system 2 Kistler frce plates (Calibrated Anatomical System Technique) Eight-channel TELEMG electromyograp h REV 9000 dynamometer (IKS, International Knee Society)	3 walk trials Voluntary muscle contraction knee joint at 90, 70, 45, 20°. Bilateral.	No	This study found that total knee replacement (TKR) for proximal tibia tumors often results in abnormal gait patterns characterized by extensor weakness and knee extension lag. Conversely, osteochondral allografts (AL), when optimal reconstruction is performed, yield better functional results and a higher percentage of normal knee patterns during gait

Zohman et al., 1997	Gait	Bone Tumor: Proximal Tibia (10) 6.5 years [PTR (10), AKA (5)]	PTR vs. AKA	Foot pads B&L Stride Analyzer (B&L Engineering, Santa Fe Springs, CA) 10m walkway 2 Photocells	Each subject performed 4 walking trials. Results were averaged.	Extensor lag with gait velocity, cadence or stride length, stance simmetry	The study found that gait after intraarticular proximal tibial replacement (IPTR) is comparable to that after above-knee amputation (AKA) with an external prosthesis, with its parameters (velocity, cadence, stride length) being similar to those of normal subjects. Furthermore, a greater extensor lag in the IPTR group was negatively correlated with stance time symmetry, indicating that extensor mechanism dysfunction contributed to asymmetric gait

The average age of the study populations falls within adulthood. However, some groups also include pediatric patients, starting from 11 years of age. No studies focused exclusively on pediatric or elderly populations. The mean time from intervention in the included studies ranges from approximately one month (4.9 weeks) to 14 years.

Five studies focus on comparisons between patients who underwent PTR and those who underwent procedures for tumors in other anatomical locations, most commonly DFR. Three studies focus exclusively on patients with PTR, one of which compares two different surgical techniques. The sample size for PTR groups ranges from 5 to 10 patients. The only two studies assessing balance included mixed samples of patients with both PTR and DFR.

Gait Analysis:

Setup & Task

In five of the six studies focused on gait domain, gait analysis was conducted using optoelectronic motion capture systems. The instrumentation typically includes multi-camera infrared emission systems synchronized with force platforms to capture 3D kinematic and kinetic data (Almeida et al., 2024; Colangeli et al., 2007; Fowler et al., 2021; Kim et al., 2021b), with some studies also employing isokinetic dynamometers for quantitative muscle strength assessment (Colangeli et al., 2007; Fowler et al., 2021; Pilge et al., 2015). Only one study (Zohman et al., 1997) employed a wearable stride analyzer and a 10-meter walking path. Patients typically walked either on a treadmill (Pilge et al., 2015) or overground (Almeida et al., 2024; Fowler et al., 2021; Kim et al., 2021a) along a straight path of 7 to 10 meters. In other studies, such as Colangeli et al., (2007), the walking distance was not reported. Where specified, the task generally involved subjects walking barefoot at a self-selected, comfortable pace along a straight walkway, with multiple walking trials averaged for analysis (Almeida et al., 2024; Fowler et al., 2021; Kim et al., 2021b; Zohman et al.,

1997). In only one study, patients walked at both a self-selected and a fast walking speed (Fowler et al., 2021). For such analyses,

Parameters

Among the gait cycle parameters analyzed were spatiotemporal parameters (gait speed, cadence, gait cycle time, stance and swing duration, double support duration, step and stride length), joint angles, joint moments and power at the knee, hip, and ankle, as well as ground reaction forces (GRFs). These parameters were assessed either for the operated limb only or for both the operated and the contralateral (unaffected) limb.

Results

Gait analysis studies investigating functional outcomes following knee endoprosthesis after bone tumor resections consistently report altered gait parameters compared to healthy individuals. The main results consistently indicate reductions in gait speed, stride length, and cadence, as well as an increase in support time in operated groups compared to controls (Almeida et al., 2024; Colangeli et al., 2007; Fowler et al., 2021; Kim et al., 2021b; Zohman et al., 1997). Specifically, for PTR, a recurrent finding is extensor mechanism dysfunction and weakness, leading to specific gait abnormalities. Notably, Zohman et al. (1997) found an inverse correlation between increased extensor lag (a partial or complete loss of the ability to actively extend the knee, although complete passive extension is possible) and stance time symmetry. Colangeli et al. (2007) reported a higher incidence of knee extension lag and a prevalent stiff/hyperextension knee gait pattern with reduced rectus femoris activity in patients with total knee replacement (TKR), along with a significant reduction in knee extensor muscle strength. Pilge et al. (2015) similarly reported a mean extensor lag of 1° and reduced mean extensor muscle strength (25.8% of the non-operated leg), resulting in a stiff knee gait pattern. Fowler et al. (2021) also identified slight knee hyperextension throughout most of stance, leading to reductions in mean peak knee angle, moment, and power generation, and altered ankle biomechanics (excessive plantar flexion, reduced plantar flexor moment), attributed to ankle muscle resection and transposition. Despite these deficits, Fowler et al. (2021) concluded that walking speed and quality of life were relatively normal. Concordances among studies also include the finding that both operated groups (distal femoral resection (DFR) and PTR) show abnormal ground reaction forces (GRF) compared to controls, typically with reduced anteroposterior and vertical forces (Almeida et al., 2024; Kim et al., 2021b). However, some differences were observed between DFR and PTR

groups. While Almeida et al. (2024) concluded that no major statistically significant differences were found in kinetic and kinematic parameters between the operated groups, although DFR showed a cadence closer to the control than PTR (Almeida et al., 2024), Kim et al. (2021b) compared PTR and DFR, and identified distinct differences in kinematic and kinetic patterns depending on the tumor location (Kim et al., 2021b). Specifically, the PTR group tended to maintain a flexed hip throughout the gait cycle compared to the DFR group's tendency for greater hip extension (Kim et al., 2021b). Kim et al. (2021b) also noted a higher maximal knee flexor moment during midstance and lower maximal plantarflexion moment in the PTR group compared to DFR, suggesting that rehabilitation strategies should be differentiated based on tumor location.

Proximal tibial tumors can be managed using different reconstructive techniques, including proximal tibial replacement, allografts, and total knee replacement endoprostheses. Therefore, comparing functional outcomes across these surgical approaches is important to better understand gait impairments and to inform surgical decision-making and rehabilitation strategies. Colangeli et al. (2007) concluded that allografts implants showed better functional results than TKR endoprostheses, attributing knee kinematic abnormalities in TKR to extensor apparatus weakness and intrinsic implant mechanics (Colangeli et al., 2007), while Pilge et al. (Pilge et al., 2015) found good functional outcomes with their reconstruction technique (patellar-loop technique). These variations highlight the complexity of gait outcomes, influenced not only by resection location but also by specific surgical techniques and reconstruction challenges.

Limitations

A primary concern across most sources is the small sample size, which limits statistical power and constrains analyses to observable differences only (Almeida et al., 2024; Colangeli et al., 2007; Fowler et al., 2021; Kim et al., 2021b; Pilge et al., 2015), largely due to the rarity of proximal tibial tumors and associated high mortality (Pilge et al., 2015). Selection bias is another recurring issue, as patients with better functional outcomes were more likely to participate, while the complexity of surgery and lengthy rehabilitation discouraged broader inclusion (Almeida et al., 2024; Fowler et al., 2021; Kim et al., 2021b). Follow-up duration varied widely between subjects and comparison groups, affecting consistency in outcome interpretation (Almeida et al., 2024; Colangeli et al., 2007; Kim et al., 2021b). Moreover, muscle activity and strength data were often limited, with sparse use of EMG and incomplete profiling of key muscle groups (Kim et al., 2021b), although some

studies employed MMT or dynamometry (Fowler et al., 2021). Longitudinal studies were also affected by heterogeneity in surgical techniques and prostheses, introducing variability in outcomes due to evolving practices and materials (Pilge et al., 2015).

PA Levels:

Setup & Task

Three studies focused on PA. The PA levels were assessed using a stepwatch activity monitor worn above the ankle for one week (Bernthal et al., 2015; Fowler et al., 2021) and a portable breath-by-breath pulmonary gas exchange unit (Bernthal et al., 2015), or a pedometer worn for 2 weeks (Sugiura et al., 2001).

Parameters

The parameters assessed were the total number of strides measured (Fowler et al., 2021), the total number of strides/steps per day (Fowler et al., 2021; Sugiura et al., 2001), cadence (Fowler et al., 2021) or the mean number of strides per day, gait velocity and oxygen consumption (Bernthal et al., 2015).

Results

Patients undergoing endoprosthetic reconstruction for primary lower extremity bone sarcoma, specifically those with PTR, generally demonstrate efficient gait and active lifestyles in both home and community environments, even at long-term follow-up (Bernthal et al., 2015; Fowler et al., 2021). Objectively, PTR patients have been reported to achieve a mean of 4411 strides per day (Bernthal et al., 2015) or 4564 ± 1514 strides per day (Fowler et al., 2021), which was not significantly different from other lower extremity reconstruction groups or control groups, respectively (Bernthal et al., 2015; Fowler et al., 2021). When converted to steps per day (approximately 9128 steps/day), this activity level is considered similar to that of adults without disability (normative data of 9448 steps/day) (Fowler et al., 2021). In a broader study encompassing various bone tumors, including five proximal tibia cases, patients averaged 6001 steps per day, with those undergoing Kotz Method Total Knee Replacement (KMFTR), a type of PTR, tending to show lower step counts compared to other reconstruction methods (Sugiura et al., 2001). Despite comparable average daily stride counts and normal walking speeds observed in laboratory settings (Bernthal et al., 2015; Fowler et al., 2021), specific gait abnormalities persist. PTR surgical limbs exhibit significantly decreased single limb support time, reduced heel rise during terminal stance,

and an absence of normally occurring knee flexion angles, extensor moments, and power generation during initial double limb support (Fowler et al., 2021). A reduced peak plantar flexor moment is also observed (Fowler et al., 2021). These biomechanical deficits are consistent with documented severe knee extensor and ankle plantar flexor weakness (Bernthal et al., 2015; Fowler et al., 2021). Specifically, knee extension strength can be reduced by 84% and flexion by 43% in PTR patients compared to femoral reconstructions (Bernthal et al., 2015). This weakness is often attributed to surgical factors such as the use of a medial gastrocnemius flap and disruption of the extensor mechanism (Bernthal et al., 2015; Fowler et al., 2021). Furthermore, during community walking, the PTR group demonstrates a significantly higher percentage of low-frequency strides (5.3% greater) compared to controls, suggesting an influence of underlying weakness or fatigue on their typical walking patterns (Fowler et al., 2021). Nevertheless, despite these specific gait abnormalities and strength deficits, the overall impact on community walking and health-related quality of life is considered relatively mild, with quality-of-life scores often exceeding U.S. national averages (Fowler et al., 2021).

Limitations

The studies on functional outcomes following endoprosthetic reconstruction for lower extremity bone sarcoma present several limitations. A significant potential for selection bias exists, as patients who are more content with their surgical outcomes may be more inclined to volunteer for functional assessments, potentially skewing results towards more optimal outcomes (Bernthal et al., 2015; Fowler et al., 2021). The variability in required muscle resection due to differing tumor sizes also makes comparisons challenging, with patients undergoing more extensive resections (who would presumably be less functional) potentially less likely to return for analysis, further influencing the data positively (Bernthal et al., 2015). Both studies acknowledge relatively small sample sizes, particularly for certain objective measurements like "Step Watch" activity data, which may limit the generalizability and statistical power to detect all potential gait abnormalities, necessitating larger prospective trials to overcome this limitation (Bernthal et al., 2015; Fowler et al., 2021). Discrepancies in comparing activity levels to historical controls are also noted due to variations in how gait metrics (e.g., steps versus strides) are defined and reported, underscoring the need for standardized methodologies in future research (Bernthal et al., 2015). Additionally, differences in study follow-up periods and measurement techniques

(e.g., oxygen consumption methods) can complicate direct comparisons with previous research (Bernthal et al., 2015).

Balance:

Two studies analyzed postural control abilities. However, the sample studied was composed of a mixture of PTR and DFR patients, making it impossible to isolate the results for PTR patients alone.

Setup, Task & Parameters Measured

The measurement of balance control was conducted using stabilometric platforms, wherein patients were instructed to stand upright for a duration of 10 or 30 seconds, with and without their eyes open (Morri et al., 2019, 2018). The speed of the center of pressure (SCoP) (mm/s) was measured. The 10-meter test was utilized to assess gait speed, while the 6-minute walk test (6MWT) was employed to evaluate gait resistance. The timed up and go (TUG) test was employed to evaluate mobility, with the time taken to complete the task serving as the primary outcome measure (Morri et al., 2019, 2018).

Results

A cross-sectional study examining functional recovery one year after modular knee endoprosthetic reconstruction revealed a strong association between balance control and objective measures of gait performance (Morri et al., 2018). The primary objective of this investigation was to determine which factors contribute to functional recovery in patients who underwent resection of a bone tumor in the distal femur or proximal tibia (Morri et al., 2018). The speed of the Centre of Pressure (SCoP), which is utilized as an index of the activity required to maintain stability, demonstrated a significant correlation with all specific gait tests performed (10m-test, time used to walk a 10m distance; 6MWT, maximal distance walked in 6 minutes) (Morri et al., 2018).

Morri et al. (Morri et al., 2018) found that SCoP measured with eyes open exhibited a robust positive correlation with the 10-meter walking test (10m-test,) and a significant negative correlation with the 6MWT. As indicated by Morri et al. (2018), similar strong correlations were observed when SCoP was measured with eyes closed.

Also, the SCoP with eyes open demonstrated a significant correlation with the Time Up and Go (TUG) test (Morri et al., 2018).
Therefore, these results underscore the notion that heightened difficulty in managing balance is systematically associated with diminished gait performance, encompassing aspects such as speed, resistance, and mobility.
Additional factors have been identified as contributing to the issue. The study also found that age, the duration of chemotherapy, and the strength of the knee extensor muscles demonstrated correlations with functional outcomes. Specifically, the strength of the knee extensor muscles was found to be significantly correlated with the subjective Musculoskeletal Tumor Society (MSTS) rating scale score (Morri et al., 2018). However, a lack of significant correlation was observed between muscle strength and objective gait tests. In contrast, joint Range of Motion (ROM) and the percentage of bone resection did not demonstrate a statistically significant correlation with functional gait tests (Morri et al., 2018). Notably, balance control (SCoP) did not seem to be linked to subjective disability indices, including the MSTS score and the Toronto Extremity Salvage Score (TESS).

A subsequent controlled observational study evaluated the effectiveness of integrating specialized balance training, utilizing Serious Games (e.g., the Wii Fit Balance Board), into the rehabilitation protocol for patients following knee resection and modular prosthetic replacement (Morri et al., 2019). The Study Group received 25 minutes of targeted postural and proprioceptive training per session, while the Control Group received standard strength and ROM exercises.
A statistically significant improvement in walking speed (10 mWT) was achieved by the study group. The median walking speed for the study group was 1.48 m/s, compared to 1.26 m/s in the controls, resulting in a median difference of 0.22 m/s. This result aligns with the walking speed calculated for healthy individuals in the same age range (Morri et al., 2019).
A substantial enhancement in postural control was observed, as indicated by the mean oscillation speed of the Center of Mass (SCoP) in the standing posture. The median SCoP of the study group was found to be significantly lower than that of the controls, with a median of 9.3 mm/s. Lower SCoP has been demonstrated to be associated with enhanced postural stability (Morri et al., 2019).
While the TUG test execution time was reduced in the study group by a median of 1.4 seconds, this difference was not statistically significant (Morri et al., 2019). Moreover, the tailored balance training approach did not show improvements in comparison to the standard

protocol with regard to recovery of knee range of motion (ROM), muscle strength, MSTS score, or TESS score. No significant differences were observed between the groups for these variables (Morri et al., 2019). Also, the study group demonstrated a superior outcome in walking endurance (6mWT), although this was not statistically significant (Morri et al., 2019).

The present study arrives at the overall conclusion that rehabilitation incorporating exercises aimed at recovering motor control and balance, particularly those utilizing Serious Games, can effectively enhance objective gait recovery and postural control in patients following modular prosthetic surgery. This finding aligns with the notion that rehabilitation should encompass more than merely addressing individual deficits, such as strength and joint mobility, but rather should extend to the comprehensive consideration of the sensorimotor system in its entirety.

Limitations

The most significant limitation was the small sample size of the first study, which precluded the opportunity for a more in-depth statistical analysis, particularly an inferential analysis with the necessary statistical power (Morri et al., 2018). The authors explicitly noted that the rarity of the bone tumor disease significantly influences the feasibility of designing research protocols on larger, more uniform samples required for multivariate statistical analyses (Morri et al., 2018). Moreover, the observation group included patients undergoing resection of both the distal femur and the proximal tibia. This reconstruction involves different biomechanical and anatomical elements. While only 3 out of 15 patients underwent proximal tibia resection, this surgical variability adds complexity to the interpretation of functional outcomes (Morri et al., 2018). Additionally, the evaluation of postural control was achieved by measuring the Speed of the Centre of Pressure (SCoP) using a stabilometric platform (Morri et al., 2018). The authors' decision to administer the test for a mere 10 seconds was identified as a particular limitation of the study. It was also noted that there is currently a lack of uniformity in the literature regarding the methodology for this testing, making it challenging to define a standard mode of execution (Morri et al., 2018).

6.1.4 Literature Gap

The aim of the present literature review was to summarize the current evidence on objective assessments of gait, physical activity, and balance in proximal tibial replacement patients, and explore potential interrelationships among these functional domains.

A review of the extant literature reveals a scarcity of studies that integrate and correlate gait, physical activity levels, and balance. The relationship between patients' motor skills, measured in a controlled environment, and their motor habits in everyday life, measured in an ecological environment, remains unclear. While there are studies on the biomechanical analysis of gait in PTR patients, albeit limited by the small sample size due to the rarity of this condition, the number of studies measuring physical activity levels is even smaller, making this area less explored. Additionally, the collected data prioritizes the number of steps taken per day, while disregarding crucial information such as the duration of sitting or standing bouts, recognized as potential health risk factors. Conversely, the balance abilities of this specific patient population have not been adequately explored, necessitating further research in this area. However, there is a general absence of a comprehensive perspective on the psychophysical state of patients that considers both biomechanical and postural control aspects, as well as lifestyle habits and quality of life. The lack of integration of both objective information and subjective reported outcomes provide an incomplete representation of the health status of this category of patients one year or more after surgery. This approach would have the potential to enhance the oncological and rehabilitation process for patients by facilitating targeted rehabilitation programs and enhancing post-operative care.

6.2 Gait and Physical Activity in Patients with Proximal Tibial Replacements after Musculoskeletal Tumours: Preliminary Data

Based on the insights gained from the literature review of this specific patient population, this chapter describes the methodology and exploratory application of the STOMP protocol during my training at the Royal National Orthopaedic Hospital (RNOH) in London. It provides an overview of how the protocol was implemented in this context and offers preliminary observations on the collected data and considerations that emerged from this initial experience. Since data collection is ongoing, the discussion presented here should be regarded as preliminary and descriptive.

6.2.1 Proposed Methodology

Study Design and Participants

A cross-sectional pilot study was conducted using data from the STanmore OutcoMes Project (STOMP). Patients who had undergone proximal tibial replacement (PTR) for oncological indications were recruited during routine follow-up visits. Eligibility criteria included: patients at least one year post-surgery, able to walk independently without assistive devices. Patients were excluded from the study if they met any of the following criteria: (1) ongoing chemotherapy or radiotherapy, (2) postoperative complications affecting mobility (e.g., infection, mechanical failure, revision surgery), or (3) comorbidities significantly impairing gait.

Gait Analysis

Spatio-temporal gait variables and lower-limb joint kinematics and kinetics were assessed using Motek's Gait Real-time Analysis Interactive Lab (GRAIL; Motek Medical, The Netherlands). The GRAIL system integrates a dual-belt instrumented treadmill, a 180° virtual reality environment, and a multi-camera motion capture system synchronized with force platforms. Participants walked at a self-selected comfortable speed following a standardized acclimatization protocol. Spatio-temporal parameters (e.g., gait speed, step length, cadence), three-dimensional joint angles, and joint powers of the hip, knee, and ankle were extracted for analysis.

Daily Physical Activity

The participants' daily physical activity (PA) and sedentary behavior were assessed using the ActivPAL™ device (PAL Technologies Ltd, Glasgow, Scotland). Participants were required to wear the device continuously on the anterior thigh for a minimum of seven consecutive days. The raw accelerometry data were processed with ActivPAL software to quantify the following: step count, time spent in sedentary and upright postures, standing, and stepping.

Patient-Reported Outcome Measures (Adults and Children)

Subjective functional outcomes were assessed using age-appropriate, validated questionnaires. The following instruments were administered to adult participants. The Toronto Extremity Salvage Scale (TESS) (scale 0-100), employed for the evaluation of disability in daily activities. The Quality of Life–Cancer Survivors (QoL-CS) scale (scale 0-10), to assess the multidimensional quality of life of cancer survivors. The modified Reintegration to Normal Living (mRNL) index (scale 0-100), to quantify perceived reintegration into social and community life.

The functional status and quality of life of pediatric participants were assessed using the following instruments. The BT-DUX (Bone Tumor–Dutch Questionnaire) (scale0-100), a self-reported measure developed for children and adolescents treated for bone tumors. The Pediatric Outcomes Data Collection Instrument (PODCI) – Patient Version, and the PODCI (parent proxy version) (scale 0-100), in which parents provide parallel evaluations of their child's functional abilities and daily participation.

6.2.2 Overview of Preliminary Results

Initially, clinicians identified ten eligible patients treated with proximal tibial replacement, of whom eight consented to participate and were enrolled in the study. All participants who were recruited completed the patient-reported outcome measures. Five participants underwent gait analysis, while six completed the ActivPAL assessment. The predominant reasons for non-attendance at the hospital-based gait assessment were travel distance and, for a subset of those who declined participation, a combination of distance and ongoing therapies.

The analysis included a total of eight patients, with a median age of 26 years and a range of 14 to 74 years. The duration since surgery ranged from one to seven years, with a median

duration of 3 years. It is noteworthy that none of the participants were undergoing chemotherapy at the time of assessment.

The results of the PROMs are shown in Table 9, the results of the gait spatiotemporal parameters are reported in Table 10, and knee and ankle kinematics and kinetics are shown in Figure 8. Daily physical activity results are reported in Table 11.

Table 9 *– Summary of patient-reported outcome measures (PROMs), including functional status, quality of life, and reintegration into daily living for adult and pediatric patients. Results are reported for the TESS, QoL-CS, mRNL, BT-DUX, and PODCI (patient and parent proxy.*

Patient	**Diagnosis**	**Category**	**TESS**	**QoL**	**mRNL**	**PODCI** Patient	**PODCI** Parent	**BT-DUX**
1	Osteosarcoma	Child				34	36	-
2	Ewings	Child				39	30	26
3	Osteosarcoma	Child				40	24	34
4	Osteosarcoma	Adult	94	7	100			
5	Osteosarcoma	Adult	45	1	39			
6	Telangiectatic Osteosarcoma	Adult	84	5	97			
7	Leiomyosarcoma	Adult	57	5	42			
8	Chondrosarcoma	Adult	48	5	61			
Median			57	5	61	39	30	30

Table 10 *– Patients gait spatiotemporal parameters are reported.*

Patient Number	Gait Speed (m/s)	Cadence (steps/min)	Step Length S (m)	Step Length H (m)
1	0.84	114.5	0.50	0.44
3	1.11	98.6	0.67	0.70
4	0.81	101.9	0.45	0.43
6	0.55	91.8	0.39	0.36
8	0.53	98.6	0.37	0.32
Median	0.81	99.0	0.45	0.43

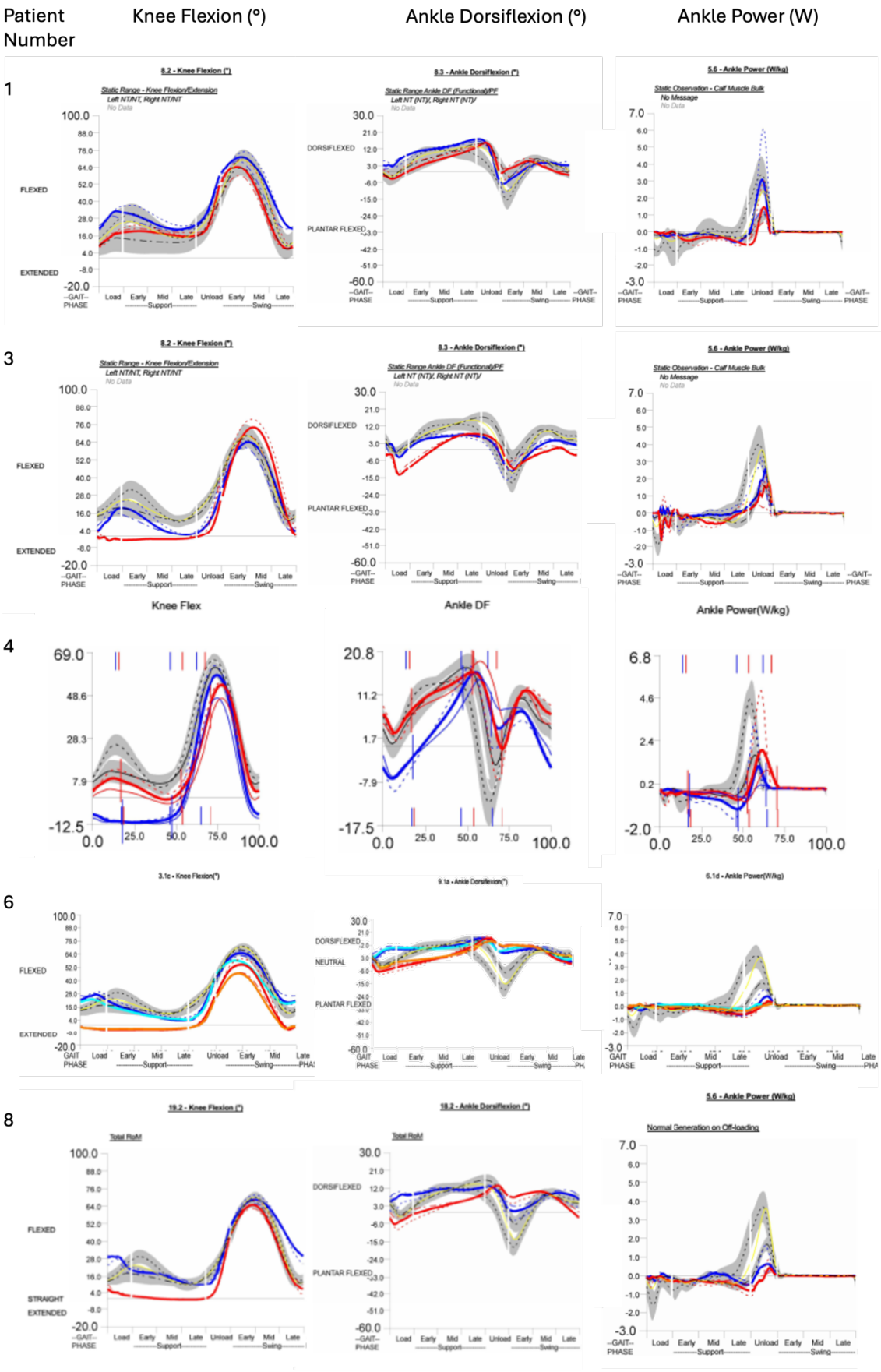

Figure 8 *– Knee flexion, ankle dorsiflexion and ankle power are displayed. In patients 1, 3, 6, and 8 the red line represents the surgical limb and the blue line the healthy limb. In patient 4 the blue line represents the surgical limb and the red line the healthy limb. Grey color represents normative values. For all graphs, the x-axis represents the gait cycle (support phase*

and swing phase), while the y-axis shows the measured parameter. The first column displays knee flexion angles (°) for each patient, the second column shows ankle dorsiflexion angles (°), and the third column reports ankle power (W). Each line represents an individual patient's data across the gait cycle.

***Table 11** – Daily physical behavior outcomes derived from ActivPAL monitoring in the patient cohort. Values represent average daily measures for each participant; the final row reports the group median for each parameter.*

Patient N.	Steps per Day	Cycling Steps per Day	Standing Time (min)	Stepping Time (min)	Cycling Time (min)	Sitting Time (min)	Seated Transport Time (min)	Lying Time (min)	N. Sit to Stand Transitions	Activity Score (MET.h)
1	8820	0	172	987	0	587	252	247	43	339
3	13483	55	232	164	0.7	469	70	32.57	56	359
4	4675	1040	242	624	694	569	984	47.32	35	32.45
6	7409	0	202	100	0	549	235	0.45	68	334
7	1832	0	493	348	0	804	0	269	59	31
8	5591	0	224	725	0	672	33	696	43	328
Median	6500	0	228.19	486.46	0	578	152.64	147.37	49.5	330.96

6.2.3 Considerations

The patient-reported outcome measures in the present cohort indicate moderate functional limitations and a variable perception of quality of life among adult patients following proximal tibial replacement. Specifically, the median TESS score was 57 (range 45–94), reflecting residual physical impairments in daily activities. This variability is coherent with previous studies (Graulich et al., 2021). while the median QoL-CS score was 5 (range 1–7, scale 0–10), indicating a moderate overall quality of life. The mRNL index demonstrated a median value of 61 (range 39–100), indicating partial reintegration into normal living. This finding underscores the notion that patients may persist in encountering challenges in achieving full participation in social and community activities even one year or more following surgery. Quality of life and return to normal living scores were slightly lower than previous reports (Fowler et al., 2021; Nagarajan et al., 2004).

In the pediatric and adolescent subgroup, PROMs revealed markedly lower scores, suggesting a more pronounced impact on both the functional and psychosocial domains. The median PODCI patient score was 39 (range 34–40), while the PODCI parent proxy reported a median of 30 (range 24–36). Similarly, the BT-DUX median score was determined to be

30 (range 26–34). These values indicate a substantial perceived disability and confirm a psychosocial impact of the surgical procedure, affecting not only the patients' self-perception but also the caregivers' assessment of their child's functioning. The consistency observed between patient and parent reports reinforce the reliability of the findings. These results were lower than previous studies on bone sarcoma patients (Frances et al., 2007). However, there is a lack of studies on this topic in this specific population in the literature, which makes it difficult to interpret the results for this category.

While adults appear to experience moderate limitations, younger patients and their families report greater functional and psychosocial challenges. This highlights the need for age-appropriate interventions aimed at optimizing recovery, quality of life, and reintegration into daily activities.

Gait analysis in patients with proximal tibial replacement (PTR) revealed an impact on gait spatiotemporal parameters. Coherently with previous studies (Kim et al., 2021b), participants exhibited reduced gait speed and lower cadence compared with normative values, reflecting a conservative gait pattern likely adopted to enhance stability and reduce joint loading. Step length was decreased bilaterally, further contributing to the reduced walking speed.

Kinematic and kinetic patterns that are largely consistent with previous reports in the literature. Specifically, knee joint motion during the stance phase exhibited a tendency toward greater extension, indicative of a compensatory strategy of the lower limb in the absence of normal quadriceps function, following surgical reconstruction. This pattern has been similarly observed in prior studies (Almeida et al., 2024; Kim et al., 2021b), where PTR patients exhibited reduced knee flexion excursion throughout stance and a relative “stiffening” of the knee to maintain support during weight acceptance.

Subtle reduction in ankle dorsiflexion during mid-stance was observed, which may serve as a compensation for calf muscle weakness, which is also confirmed by the reduced push-off power (Okita et al., 2014b). At the ankle joint, participants exhibited reduced plantarflexor power during push-off, which is consistent with the prevailing finding of impaired energy generation in the distal segment following proximal tibial surgery. The diminished ankle power is indicative of a limited contribution to forward propulsion, possibly due to altered muscle-tendon mechanics or protective gait adaptations. These findings were consistent with previous studies (Almeida et al., 2024; Kim et al., 2021b).

Taken together, these findings suggest that, despite variations in surgical technique and time since surgery, PTR patients consistently exhibit a gait characterized by relatively extended knees during stance, reduced ankle power, increased ankle dorsiflexion, slower gait speed, lower cadence, and shortened step lengths. This observation supports the notion that distal joint function adapts to compensate for structural and functional changes.

A comprehensive analysis of the ActivPAL data revealed substantial heterogeneity in daily physical behavior across participants. In general, the subjects exhibited a decrease in ambulatory activity, with a median of 6,500 steps per day, which are slightly below the global threshold, according to previous metanalysis (Bohannon, 2007). However, these numbers might change according to age or country lifestyle (Bohannon, 2007). It also must be noted that some values, as low as 1,800 steps per day, are significantly below the thresholds typically reported for healthy adults. Besides, these numbers do not meet the recommendations for a healthy lifestyle which suggest 10.000 steps/day (Tudor-Locke and Bassett, 2004). The variability exhibited by the step time reflected substantial functional heterogeneity, which likely reflected differences in surgical history, residual muscle capacity, and individual adaptation to the prosthesis. The prevalence of cycling was minimal, indicating a limited engagement in low-impact activities that could potentially offset the decline in walking tolerance. Sedentary behavior was prominent, with a median sitting time exceeding 9.5 hours per day, consistent with national UK average levels (UK Parliament). However, these numbers represent a significant risk factor (Booth et al., 2012). which might augment other critical conditions that may be present in this population regarding bone health or cardiovascular disease (Chen et al., 2022; Rizzoli et al., 2013). Furthermore, the duration of lying varied considerably, which could be indicative of increased rest requirements, pain management strategies, or fatigue related to long-term functional limitations after PTR. The number of sit-to-stand transitions (median 49.5/day) fell within the average functional range assessed by previous studies (Bohannon, 2015). Collectively, these findings depict a pattern of reduced mobility, high sedentary exposure, and limited engagement in alternative physical activities. These results underscore the necessity for long-term activity-support strategies aimed at increasing daily mobility and reducing sedentary time in this patient group.

The present study demonstrates that, despite the presence of similarities in functional patterns, patients' perceptions of quality of life and daily activity habits may differ. Due to the limited sample size, stratification by age groups was not possible, representing a

limitation. Another potential limitation is selection bias, as patients who are relatively more active and have fewer functional deficits may have been more likely to participate, thereby limiting the generalizability of the findings to the broader patient population. Moreover, the rarity of the condition imposes limitations on the capacity to recruit sufficient numbers, thereby hindering the attainment of adequate statistical power.

Further research is necessary to expand the study's population sample and to examine the data with respect to age demographics.

6.2.4 Concluding Remarks

Adult patients undergoing proximal tibial replacement experience persistent moderate functional limitations and partial reintegration into daily life one year or more after surgical intervention, as reflected by patient-reported outcome measures. Younger patients, including children and adolescents, exhibit more significant functional and psychosocial impairments, thereby emphasizing the considerable impact of surgery on both the self-perceived and caregiver-reported quality of life.

Gait analysis reveals a characteristic pattern among PTR patients, including reduced gait speed, lower cadence, shortened step length, increased knee extension during stance, and diminished ankle power. These adaptations are indicative of compensatory strategies employed to maintain stability and forward progression in the presence of altered muscle-tendon function and reconstructed extensor mechanisms.

Objective activity monitoring has been revealed to demonstrate considerable heterogeneity in daily physical behavior, with reduced ambulatory activity, prolonged sedentary periods, and limited engagement in alternative low-impact exercises. These findings underscore the long-term ramifications of PTR on overall mobility and underscore the significance of interventions designed to augment daily activity and limit sedentary behavior.

Taken together, these results emphasize the need for individualized rehabilitation strategies that address not only functional recovery but also psychosocial well-being. Such strategies should focus on optimizing mobility, enhancing gait mechanics, and supporting reintegration into daily and social activities. As a future perspective, studies exploring relationship between clinical assessments and real-world physical activity behaviour would be essential for improving our ability to interpret and integrate these measures in clinical practice.

Overall, this study offers a comprehensive assessment protocol that provides a holistic view of the patient's physical and psychological health. This protocol can serve as a valuable tool to inform clinical decision-making and guide tailored patient support.

Chapter 7 – General Discussion and Conclusion

This chapter summarizes the key findings presented throughout the thesis and critically interprets their relevance within the broader fields of orthopedic oncology and patient management. The chapter also examines the study's methodology, acknowledges its limitations, and considers the implications for clinical practice and future research. Additionally, the chapter summarizes the work's primary contributions, highlighting their scientific and clinical value, and outlines potential directions for further investigation and clinical application.

7.1 Summary of The Main Findings

This doctoral research examined the potential of wearable sensors to objectively evaluate motor function in individuals with muscoloskeletal tumors and enlighten their integration into clinical practice. The objective was to assess patients motor performance in a more ecological condition with respect to laboratory-based method, using a wearable assessment protocol. The study applied this protocol to characterize movement patterns that are often difficult to detect through conventional clinical evaluations.

The first study, presented in chapter 2, consisted of a literature review that examined the context of objectively assessing patients with bone and soft-tissue tumors. The review identified numerous studies that compared different types of surgical interventions and variations within the same surgical approach. These studies showed that these interventions and approaches result in distinct functional and biomechanical outcomes. However, the assessment methods employed in these studies primarily relied on laboratory-based technologies, such as motion capture systems, that require specialized equipment. This limits their accessibility and applicability in routine clinical practice. Only a few studies incorporated wearable sensor technologies. Furthermore, the literature predominantly focused on gait analysis involving straight-line walking, which provides limited insight into broader functional abilities and post-surgical consequences. The reviewed studies also indicate that kinematic and kinetic alterations occur following surgery. Though scarce, some case studies have demonstrated that individualized rehabilitation programs can lead to positive functional outcomes. Additionally, several aspects of motor performance remain under-explored, particularly functional abilities beyond straight-line gait, aspects of postural

control, and the influence of the tumor presence on the motor function prior to surgical removal.

In order to better define an assessment protocol for patients with bone and soft-tissue tumors that could be feasibly implemented in clinical settings, a methodological study, displayed in chapter 3, was required to determine how existing evaluation protocols could be adapted to the clinical environment. Clinical spaces are often limited in size and may not meet the spatial requirements necessary for certain motor assessments, which makes the direct application of standard laboratory protocols challenging. The methodological analysis revealed that the Two-Minute Walk Test can only be adapted to specific straight-line distances. When the available walking space is less than 15 meters, the test can alter gait patterns, which compromises the assessment's results.

After establishing the assessment protocol, a first study, shown in chapter 4, was conducted on patients with bone and soft tissue tumors before surgery. The patients were classified by tumor type, and their functional abilities were evaluated in three areas: gait performance, functional mobility, and postural control. The goal of this assessment was to characterize patients' preoperative motor status and explore the potential influence of tumor type and dimension on motor function. The results revealed significant differences, suggesting that the presence of bone tumors may impact gait abilities more than soft-tissue tumors. Additionally, this finding underscores the importance of including more complex motor tasks in evaluating these patients, while it appears that tumor size is not the primary cause of changes in gait patterns.

Following patients throughout their tumor care journey, a subsequent study, described in chapter 5, focused on postoperative recovery, specifically examining the influence of preexisting levels of physical activity on functional outcomes after surgery. The findings suggest that patients with more active lifestyles recovered faster, returning to preoperative functional conditions as early as six months post-surgery. In contrast, sedentary patients demonstrated altered gait patterns at the six-month follow-up, reflecting reduced dynamic stability and reduced muscle strength in the affected limb. Thus, physical activity levels may be considered predictive factors for accelerated functional recovery following surgery.

Given the considerable heterogeneity of this patient population, which complicates assessment and management, an additional study was conducted (see Chapter 6) that focused on a specific subgroup: patients who underwent surgery to remove a tumor and replace the proximal tibia. The goal was to develop and test an evaluation model that could capture patients' functional abilities and lifestyle quality after completing sarcoma treatment and

postoperative rehabilitation, more than a year after the surgery. A pilot study was conducted to comprehensively assess patients, considering not only their functional performance, but also their integration into daily life. This assessment was conducted through patient-reported outcomes (PROMs) and objective measures of gait performance and physical activity levels. The preliminary data revealed considerable variability in patients perceived functional abilities and lifestyle habits, despite their relatively similar gait patterns. Data also showed that the psychosocial impact seemed to be higher on younger patients. This may suggest the need to divide the population into distinct subgroups for evaluations and rehabilitation protocols. Activity levels also varied, with some patients being more active and others being more sedentary, bringing to attention potential health risk factors. Overall, the study successfully proposed a holistic evaluation protocol that addresses multiple aspects of patients' lives after treatment. However, correlations and interaction between the studied domains remain unexplored due to the small sample size, as a consequence of the rarity of this pathology.

7.2 Discussion: Clinical Application of The Main Findings

Evaluation Protocol

This doctoral research project demonstrated and applied an assessment protocol designed to provide an objective evaluation while remaining practical and feasible in clinical settings. The findings clearly highlight the need to incorporate multiple motor tasks to comprehensively assess patients' motor abilities. In this regard, instrumented clinical tests proved to be an effective approach, as demonstrated in Chapter 4 and 5. The instrumented Two-Minute Walk Test (2MWT) was effective and well-tolerated by the examined population. It was capable of identifying different gait patterns under preoperative and postoperative conditions when test administration guidelines were followed and appropriate adaptations were made, as shown in Chapter 3. The instrumented Timed Up and Go test enriched the understanding of patients' functional abilities by incorporating more complex motor tasks, such as curvilinear walking and trunk movements, which are typically associated with common daily activities. Several parameters derived from this test were informative and allowed for the distinction of specific patient subgroups. However, the integration of additional assessment tools, such as electromyographic (EMG) analysis of muscle activation, could facilitate the identification of further specific motor deficits that

influence mobility but remain undetected or unexplained through biomechanical analysis alone. In contrast, the postural control assessment warrants reconsideration. Evaluating this ability through more challenging tasks (beyond simple static balance with eyes open) may provide clinically relevant information, as demonstrated in previous studies (de Visser et al., 2001; Morri et al., 2019). Examples may include assessing static balance with the eyes closed, testing on surfaces of varying compliance, and employing dual-task evaluations that introduce a simultaneous cognitive load.

This research underscores the essential role of wearable sensor technology in offering objective assessments. This technology provides a non-invasive, well-tolerated, and rapid evaluation method. Placing IMU sensors and administering the test battery described in the studies of Chapter 4 and 5 took an average of less than thirty minutes, making the protocol feasible for patients and clinical staff. Furthermore, wearable sensors allowed to move beyond traditional laboratory environments and conduct assessments in clinical settings without motion-analysis facilities. This flexibility allows the protocol to be easily adapted to available physical spaces of the clinics and paves the way for future evaluation procedures conducted in real-life environments. For assessments requiring the patient's presence at the hospital, instead, scheduling the functional evaluation tests alongside the medical staff's already-planned routine follow-up appointments was an effective solution to enhance patients' adherence to the study. Concomitantly, this strategy further demonstrates the ease with which the proposed protocol can be implemented and integrated into everyday clinical practice. Using wearable physical activity monitors, to evaluate patients' lifestyle habits in real-life conditions was also effective, as demonstrated in Chapter 6. Patients tolerated the device well, and its ease of self-application, combined with the ability to mail it directly to participants, enabled the inclusion of individuals across the entire region, even those unable to travel to the hospital due to distance.

Finally, wearable sensor systems may offer advantages over traditional laboratory-based motion analysis. This is due to the fact that wearable sensor systems require less infrastructure. Indeed, these systems have the potential to reduce personnel and facility costs, as well as patient burden, suggesting that wearable assessments could provide a cost-efficient alternative suggesting potential economic benefits that warrant further investigation.

Patients' Care

The care of patients with musculoskeletal tumors is a longitudinal, multidisciplinary journey that encompasses far more than the operative phase alone.

The methodological study presented in Chapter 3 shows how test configuration can affect gait patterns and, consequently, performance and the interpretation of results. Non-standardized tests may introduce bias, reduce the reliability of the findings, and hinder comparisons across studies and different clinical environments. Ultimately, this limits our understanding of the phenomena under investigation. Therefore, this underscores the importance of standardizing tests in clinical practice. However, as previously noted, the clinical environment may pose challenges to implementing the required protocols due to unavoidable environmental or structural constraints. Thus, to ensure that test results are as reliable and comparable as possible, guidance on the potential effects of necessary adaptations is essential.

Patients with bone and soft tissue tumors exhibit a remarkably heterogeneous clinical profile, as demonstrated in Chapter 4 and 5, with factors such as tumor location and size, surgical treatment modalities, and preoperative and postoperative deconditioning levels exerting a profound influence on motor function. In this population, minor variations in performance can have important clinical ramifications, yet they are not always easily identifiable through basic or non-standardized measures. Hence the need for sensitive functional tests capable of: detecting clinically significant differences; reproducible, i.e., able to provide stable results over time and between different evaluators; and comparable, i.e., performable with uniform protocols that allow comparison between patients, centers, and studies. The first study in the thesis contributes directly to this implication, showing that even an apparently simple element such as the length of the straight line in the 2MWT can significantly alter the walking pattern, changing the number of direction changes, average speed, and step distribution. Absent standardization of the setting, comparisons between different stages of rehabilitation or between groups of patients' risk being unreliable. The sensitivity of the test is contingent not only on the parameter measured, but also on the consistency with which it is performed. The second study (Chapter 4) further reinforces this point, showing how preoperative function is influenced by specific clinical factors such as tumor type. In the absence of comparable metrics, it becomes unfeasible to ascertain whether a decline in performance can be ascribed to the disease, test variability, or extraneous confounding factors. The third study (Chapter 5) underscores an additional dimension of the aforementioned requirement: the postoperative rehabilitation process and responses to physical activity can only be accurately assessed if the tools employed possess sufficient sensitivity to detect progressive improvements and reproducibility to enable comparisons with previous measurements of the same patient. Therefore, only through sensitive,

reproducible, and comparable assessment is it possible to identify the patient's real needs, monitor the course of the disease and recovery, and accurately evaluate the effectiveness of rehabilitation interventions and surgical strategies.

Preoperative function is a key element in the management of patients with bone and soft tissue tumors. Prior to surgery, these patients often present with a combination of clinical and biomechanical factors that can negatively affect functional performance: pain, mechanical limitations due to the tumor, alterations in posture and motor patterns, reduced physical activity, and general deconditioning. Identifying the main determinants of preoperative function is essential because these factors not only describe the current functional status but can also predict postoperative progress and response to rehabilitation.

As shown in Chapter 4, this research shows that, in this specific populations the presence of muscoloskeletal tumor influences motor function prior to surgery. However, it is related mainly to tumor type, rather than tumor size. These results underscore the relationship between the functional differences observed preoperatively and the specific clinical characteristics of the condition, helping to differentiate patients' subgroups. Secondly, it underscores the necessity for a comprehensive preoperative assessment that transcends a qualitative description, emphasizing the incorporation of quantitative and standardized measures. These results are consistent with qualitative research showing that patients with bone tumors report poorer physical functioning, compared to patients with soft tissue tumors (Kruiswijk et al., 2023). However, this previous research did not provide descriptive data on the movements examined, which makes the functional outlook for these patients unclear. Therefore, these measures proved to be essential for discerning subtle variations in impairment levels among patients. This will allow preoperative treatments to be targeted more precisely and effectively.

However, these changes may be influenced by a number of underlying factors that have yet to be explored, such as the tumor location, i.e. proximity to the main lower limb joints or the mechanical relation and infiltration of the tumor in the surrounding tissues. In this sense, pain is certainly a key component and the most evident result of these possible interactions, but muscle deconditioning caused by altered biological metabolism (Christensen et al., 2014), and the psychological aspects linked to fear of movement and anxiety (Kruiswijk et al., 2023) also need to be investigated. Further research in this area has the potential to explain the causal mechanisms underlying these motor characteristics.

Overall, these findings underscore the importance of monitoring patients' motor function before surgery and tailoring care pathways according to individual motor abilities. In fact,

the role of preoperative determinants becomes even more relevant when they are included in a rehabilitation program. Understanding preoperative motor function can inform prehabilitation strategies and targeted motor training programs for specific patient or tumor subgroups. Patients with poorer initial function may require more intensive prehabilitation interventions, personalized support strategies or closer monitoring. One example could be the reduction of risks associated with motor impairments, such as an increased risk of falls or sedentary behavior, which are commonly reported in the literature (Rock et al., 2020). These considerations support the inclusion of motor assessments in the preoperative phase to ensure comprehensive patient management throughout the oncologic care pathway.

In addition to its role in guiding rehabilitation strategies, the objective information derived from wearable sensor-based assessments can contribute to surgical planning by providing a detailed characterization of patients' preoperative functional status. From an orthopedic perspective, the primary criteria that guide the choice of surgical approach and technique depend on tumor type, stage, location, patient general health, age, and other clinical factors (Cirstoiu et al., 2019). However, knowing a patient's functional status before surgery may add further clinical information on patients' health status useful for surgical planning. Preoperative functional capacity is an important indicator of postoperative recovery, complication risk, and overall outcomes in orthopedic and oncologic populations. Therefore, quantitative assessments of gait, balance, and functional mobility may complement traditional clinical and imaging data by offering an additional perspective on patients' physical reserve and functional vulnerability. In this context, wearable-derived outcomes can support clinicians in anticipating postoperative functional trajectories and identifying patients who may require adapted perioperative management, such as enhanced rehabilitation pathways or prehabilitation interventions. Importantly, these data do not replace established oncological or surgical criteria but rather integrate functional information into a more comprehensive evaluation framework. Establishing a reliable preoperative functional baseline may also improve the interpretation of postoperative outcomes by allowing changes in performance to be contextualized relative to patients' initial condition. By accounting for these baseline factors, clinicians could more accurately interpret postoperative progress: a patient who improves slowly may not be responding poorly to treatment but may have started from an especially compromised preoperative condition.

Following surgical treatment, for patients with bone and soft tissue tumors, postoperative motor function depends not only on the extent of the surgery or the severity of the disease, but also on pre-existing lifestyle habits and levels of physical activity. Chapter 5 of the thesis

examined this issue and found that patients who were more physically active prior to surgery, as measured indirectly through questionnaires, tended to demonstrate faster functional recovery and improved functional performance. These results suggest that baseline physical activity is an important predictor of the functional response to surgical treatment. Patients who are more active tend to have more toned muscles, better cardiovascular capacity and more efficient motor patterns, which can help to compensate for the functional loss induced by surgery. Conversely, lower preoperative activity levels may increase the risk of deconditioning and slow recovery, limiting the ability to return to daily activities. From a clinical perspective, this observation emphasizes the importance of gathering comprehensive lifestyle information from patients prior to surgery. Knowing their preoperative activity level enables to identify individuals at risk of a slow recovery and plan personalized support strategies in advance, with the aim of maximizing functional recovery.

Moreover, an active lifestyle and preoperative exercise programs may support postoperative recovery by enhancing physical fitness and functional capacity. However, the effectiveness of these programs depends on careful targeting and individualization, as demonstrated in previous studies (Wingrave and Jarvis, 2019). Moreover, some patients, particularly the frailest, may require adapted or tailored exercise interventions to meet their specific needs. A comprehensive preoperative assessment facilitates this individualized approach by enabling clinicians to identify limitations, functional deficits, and risk factors prior to surgery. Prehabilitation programs, which are designed to optimize patients' physical and functional status before surgery, could therefore improve surgical outcomes, reduce postoperative complications and accelerate recovery.

Future research should focus on exploring targeted rehabilitation and prehabilitation programs, and assessing their effectiveness, feasibility and patient adherence. The ultimate goal is to establish clear guidelines for tailoring interventions according to patients' clinical characteristics. Furthermore, the effectiveness of these interventions could be increased by extending them across multiple domains. This would encompass not only physical training, but also promoting healthy lifestyle habits, providing psychological support, and employing behavioral strategies. Integrating these complementary dimensions could help address patients' multifaceted needs, optimize adherence, and improve quality of life after treatment. In fact, the care pathway for cancer patients does not end with the postoperative phase. Rather, these individuals require continuous follow-up throughout their lives. Therefore, it is essential to understand how patients adapt to their new motor conditions in their daily lives. These conditions are shaped by altered movement patterns and permanent

compensatory mechanisms. However, the complexity of motor function in patients with musculoskeletal cancer requires an approach to assessment that is multidimensional and integrates subjective data, observable laboratory data, and data collected in the context of daily life, to provide a comprehensive picture of the patient's status. This was further explored in Chapter 6. Patient-Reported Outcomes Measures (PROMs) provide valuable information on subjective perceptions of function, quality of life, and pain. However, they can be influenced by psychological, motivational, or cultural factors. Therefore, it is necessary to integrate them with objective measures. Motion capture provides an accurate and detailed evaluation of gait patterns, balance, and joint biomechanics in a controlled environment. This method can reveal compensations or abnormalities that may not be apparent in standard clinical tests. Finally, wearables such as the ActivPAL measure motor activity in real life, providing data on daily functional behavior and actual participation in activities.

From a clinical perspective, this multidimensional approach facilitates more precise identification of residual functional deficits and personalization of patient care interventions or follow-up programs. Concurrently, it facilitates the evaluation of the impact of treatment on patients' lifestyles, particularly through the objective monitoring of physical activity levels. This approach facilitates a more nuanced interpretation of post-operative changes and a more precise comparison of the intervention's impact on the patient's daily life. It also suggests, based on the example of the previously described studies (Chapter 4 and 5), the potential and the significance of establishing a baseline of physical activity levels and daily habits to facilitate meaningful comparisons. This enables targeted interventions in areas of need related to reintegration into normal living, functional deficits, or adherence to healthy lifestyle practices. Postoperative pathways should therefore focus not only on functional recovery, but also on promoting healthy lifestyles by providing guidance on motor strategies and types of physical activity that can help patients maintain the highest possible activity level, according to their actual functional capabilities. This approach is crucial for mitigating the postoperative risks associated with sedentary behavior, which would otherwise exacerbate the elevated risks inherent to this patient population (Booth et al., 2012; Rock et al., 2020).

The findings of this thesis demonstrate that the management of patients with bone and soft tissue tumors necessitates continuous functional follow-up, extending from the diagnosis stage through the postoperative period. The methodological study on the 2MWT underscores

the importance of accurate and standardized assessment for obtaining a reliable baseline. This baseline is useful for interpreting changes after surgery and as a possible prognostic indicator, as well as provide information to clinicians useful for surgical decisions. Preoperative characterization of patients indicates that clinical factors, such as tumor type, exert a substantial influence on mobility and walking speed. This observation underscores the necessity for careful monitoring of functional progression in the weeks preceding surgery.

Postoperative studies indicate that functional recovery is non-linear and can vary considerably between patients. This underscores the necessity of regular, multimodal follow-up that integrates functional tests, instrumental measurements, and data from wearable sensors. A comprehensive approach to assessment is also underscored by the possible divergence between perceived function, potential function, and actual function in daily life, as highlighted by analysis with PROMs, gait analysis, and monitoring of daily activity.

Overall, these findings indicate that systematic functional monitoring enables the timely identification of delays or challenges, customized rehabilitation strategies, and sustained support for comprehensive and enduring recovery. This approach integrates oncological, surgical, and rehabilitative elements into a comprehensive clinical pathway that is genuinely patient-centered.

Clinical Impact of Wearable Assessments

Wearable sensor-based assessments provide objective, quantitative data that can directly inform rehabilitation delivery and clinical practice in both hospital and community settings. By capturing detailed information on gait, trunk range of motion, turn duration during the Timed Up and Go, and postural sway, these tools enable clinicians to identify specific functional deficits and monitor recovery trajectories over time.

In a hospital setting, this information can be used during follow-up visits to tailor rehabilitation interventions to individual patient needs. For example, a patient three or six months post-surgery could be assessed using the wearable system, highlighting deviations in gait symmetry, trunk mobility, or balance compared to expected recovery patterns. Based on these findings, the multidisciplinary team, including physiotherapists, orthopedic surgeons, and oncologists, can prescribe targeted exercises, adjust rehabilitation intensity, and prioritize interventions for the areas of greatest functional impairment.

In the community or home-based setting, wearable assessments facilitate remote monitoring of patients' daily activity and functional performance, allowing clinicians to track adherence,

detect early signs of delayed recovery or lifestyle behaviors that may pose health risks, and intervene promptly. By integrating wearable-derived data with patient-reported outcomes and standard clinical assessments, clinicians can make evidence-based decisions to optimize rehabilitation, prevent complications, and support long-term functional recovery.

Overall, the integration of wearable sensor-based assessments into clinical pathways enables personalized rehabilitation planning, objective evaluation of patient progress, and improved continuity of care. These tools have the potential to transform current practices by providing timely, actionable information across the entire continuum of care, from prehabilitation and early postoperative rehabilitation to long-term follow-up in hospital or community settings.

Limitations

A potential limitation of the present project is undoubtedly the considerable heterogeneity among tumor patients, due to the different tumor type, dimension and location, as well as the surgical intervention technique employed. All these aspects might limit the comparison of the data but also influence the statistical results. Moreover, the inability to divide the patients included in the presented studies into further subgroups, for instance based on type of surgery, tumor location, or age, due to the limited sample size, may have introduced bias, thereby influencing the observed results. These limitations could be addressed by recruiting larger samples. This would allow patients to be subdivided into meaningful subgroups and present statistical results both as general results of the entire sample and the results of specific subgroups, reducing the impact of the heterogeneity. However, the rarity of the pathology, combined with the possibility of losing patients due to mortality or disability related to movement, makes this particularly challenging, especially in longitudinal study designs. Therefore, multicenter studies with the capacity to recruit large patient cohorts are recommended to mitigate this issue.

Additionally, within the clinical practice, there is still a lack of an established objective evaluation protocol and clear guidelines on how to categorize patients from a functional perspective, which would be essential for conducting functional assessments while minimizing sample heterogeneity. Additionally, the evidence described in Chapter 6 revealed that meaningful differences may still exist even within narrow and well-defined categories. Thus, heterogeneity remains a major challenge in the clinical management and functional evaluation of these patient populations.

An additional methodological limitation relates to sensor placement variability. Although sensor positioning followed a standardized protocol, minor variations in placement are

unavoidable in clinical populations, particularly in patients with musculoskeletal tumors who may present with postoperative scars, pain, or anatomical alterations. Such variability may influence the accuracy of certain IMU-derived parameters, such as those related to trunk kinematics. While this reflects real-world clinical conditions, it also highlights the need for robust algorithms, standardized training for clinical staff, and further validation studies to assess the sensitivity of outcome measures to sensor placement variability.

Additional limitations are related to the patients' functional status. In many cases, it was not always possible to conduct the assessments during preoperative conditions or at follow-ups, particularly at the short-term, three-month postoperative evaluation. This was due to patients' impaired mobility, which made independent ambulation impossible and caused their exclusion from the study or missing data collection.

7.3 Conclusions and Future Perspectives

The findings of this doctoral research indicate that wearable sensor technologies provide a practical and objective approach to evaluating motor function in patients with bone and soft-tissue tumors. A series of studies demonstrated that conventional laboratory-based assessments, while precise, are often impractical in routine clinical practice and fail to capture the full complexity of patients' motor abilities. In contrast, wearable sensors facilitate real-world evaluations that are non-invasive, well-tolerated, and adaptable to both hospital and home settings, thereby offering a unique opportunity to integrate functional assessments into everyday care pathways.

This thesis demonstrates that wearable sensor-based assessments do not merely replicate laboratory measures; rather, they yield novel insights into patients' functional performance in ecological settings, capturing subtle impairments and behavioral adaptations that would otherwise go unnoticed.

From a clinical perspective, this research underscores several notable points. Firstly, it should be noted that motor impairment may be present even prior to surgical intervention, particularly in patients with bone tumors. Furthermore, this impairment does not appear to be directly related to tumor size. This underscores the necessity for preliminary, preoperative evaluation to identify impairments and develop customized interventions. A comprehensive understanding of patients' motor status prior to surgery can guide the development of prehabilitation programs, target specific motor training strategies, and potentially mitigate postoperative risks such as falls, inactivity, or delayed recovery. This finding challenges

assumptions in previous literature that functional deficits are relegated to surgery, highlighting a novel preoperative component that has been largely underexplored. Furthermore, preoperative levels of physical activity emerged as a significant factor influencing postoperative recovery trajectories, thereby suggesting their role as predictive indicators that can inform surgical clinical decisions and individualized care planning.

The studies also highlighted the heterogeneity of this patient population. Even within narrowly defined subgroups, variability was observed in activity levels and psychosocial responses. These findings underscore the necessity of a multidimensional assessment approach that incorporates objective motor measures, patient-reported outcomes, and lifestyle monitoring. In the clinical setting, the Two-Minute Walk Test and the Timed Up and Go test have demonstrated efficacy in evaluating motor abilities, capturing both fundamental and complex tasks that are pertinent to daily living. The incorporation of wearable physical activity monitors has further enhanced the ability to evaluate patients remotely, thereby increasing accessibility and adherence.

It is important to note that the application of the instrumented 2MWT and iTUG, as well as posturographic assessments, complemented by wearable sensor monitoring, in this doctoral research can be considered a proposed evaluative protocol for patients with bone and soft-tissue tumors. This framework provides a standardized, reproducible, and clinically feasible approach to monitoring functional status at several stages of the patient's treatment.

The present thesis findings also indicate that postoperative care should extend beyond traditional rehabilitation, which is focused solely on functional recovery. Emphasis should also be placed on promoting healthy lifestyle behaviors, even before the surgical treatment, supporting patients in maintaining active routines, and providing guidance on motor strategies that optimize daily-life functioning. Moreover, integrating functional and lifestyle assessments enables clinicians to obtain a comprehensive understanding of patients' needs and to design interventions that address multiple domains simultaneously.

In the future, several directions for further research are delineated. The necessity for multicenter studies is evident in order to overcome the challenges posed by small sample sizes limitations and the rarity of these tumors. Such studies would allow for subgroup analyses and greater generalizability. The assessment of postural control could be refined with more complex tasks and the integration of electromyographic measures to detect subtle deficits. Future research should also focus on further validation of wearable sensor-based assessments in patients with bone and soft-tissue tumors, to integrate additional parameters to enhance patient characterization. This process should include evaluation of concurrent

validity against reference standards and determination of sensitivity to clinically meaningful changes across the perioperative course. Validation should also be supported by algorithm refinement, as the heterogeneity of tumor types and surgical interventions may require personalized data processing to accurately capture functional outcomes across different patient subgroups. Research should also prioritize the validation of personalized prehabilitation protocols, with a focus on assessing their efficacy in enhancing both immediate and long-term outcomes. The development of standardized guidelines for integrating wearable sensors into routine clinical practice will be essential to ensure consistency, reproducibility, and wide-scale adoption.

These directions underscore how this doctoral work establishes a clear roadmap for translating sensor-based and multidimensional functional assessments into routine care, thereby providing both a scientific foundation and practical guidance for future research and clinical implementation.

In conclusion, this doctoral research demonstrates that wearable sensor-based assessments provide a feasible, objective, and clinically meaningful approach to understanding motor function in patients with bone and soft-tissue tumors. By capturing functional abilities, lifestyle behaviors, and adaptation to daily-life activities, these tools offer the potential to transform patient care. This transformation would support individualized rehabilitation, guide pre- and postoperative interventions, and ultimately improve long-term outcomes. The findings indicate a future in which real-life, sensor-based assessments become an integral component of oncological and orthopedic practice, ensuring that patients receive comprehensive, tailored support throughout their care journey. These findings demonstrate the potential for a future in which real-life, sensor-based assessments become an integral component of oncological and orthopedic practice. This would ensure that patients receive comprehensive, tailored support throughout their care journey. Furthermore, these findings could serve as a model for future research and clinical translation.

In light of the findings from this doctoral research, it is suggested that future studies explore several directions that have the potential to contribute to the advancement of both research and clinical practice. Multicenter studies are needed to overcome the challenges posed by small sample sizes and patient heterogeneity, enabling subgroup analyses and enhancing generalizability. The refinement of postural control assessments through the incorporation of more challenging tasks and complementary measures, such as electromyography, holds potential for detecting subtle deficits that may not be fully captured by conventional tests. The validation of personalized prehabilitation protocols is warranted to assess their impact

on both short- and long-term recovery trajectories. The development of standardized guidelines for implementing instrumented functional tests and wearable sensor monitoring in routine clinical practice would provide a reproducible viable framework, facilitating individualized care and continuous functional monitoring in patients with bone and soft-tissue tumors.

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