

**CROSS-SECTIONAL STUDY INVESTIGATING THE
EXERCISE BEHAVIOR, PREFERENCES, AND QUALITY
OF LIFE OF PRIMARY BRAIN TUMOR PATIENTS.**

by

ADÉL ENGELBRECHT

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**MAGISTER ARTIUM
(Human Movement Sciences)**

FACULTY OF HUMANITIES
Department of Biokinetics, Sport and Leisure Sciences at the
UNIVERSITY OF PRETORIA

Supervisor : Prof P.E. Krüger

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II

Hierdie studie word opgedra aan my ma, **Lauretha**.
(28 April 1950 – 14 Julie 2005)

Sy is gediagnoseer in 2004 met Glioblastoma Multiforme (Graad IV brein kanker). Sy was 'n inspirasie vir my en ander, deur haar positiewe en amper goddelike benadering tot hierdie siekte.

Sy het 'n moedige stryd gevoer en het bewys dat hierdie tipe kanker met behulp van ons Hoër Hand, Jesus Christus, en 'n uitsonderlike "caregiver", my pa Johan, met oorwinning gestry kan word.

This study is dedicated to my mother, **Lauretha**.
(28 April 1950 – 14 Julie 2005)

She was diagnosed with a Glioblastoma Multiforme in 2004. She was an inspiration for her positive- and almost godly approach towards this disease.

She fought bravely and she showed that being diagnosed with a brain tumor can be fought with the triumph with the help from our Heavenly Father, Jesus Christ and with the best caregiver ever, my dad Johan.

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SYNOPSIS

| | |
|------------------|--|
| TITLE | Cross-sectional study investigating the exercise behavior, preferences, and quality of life of primary brain tumor patients. |
| CANDIDATE | Adél Engelbrecht |
| PROMOTOR | Prof. P.E. Krúger |
| DEGREE | Magister Artium |

Brain tumors are the second leading cause of cancer deaths in young adults ages 20-39. (Armstrong *et al.*, 2004) According to the South African Medical Research Council, there was an estimate 801 deaths because of brain cancer in South Africa in 2000. If these statistics are compared to other types of cancers like breast-, lung- and prostate cancers, is the prevalence of the diagnoses of brain tumors, a very small percentage. According to the Mayo clinic in South Africa, the estimate number of brain tumor incidences was 3% in 2007. Despite of these statistics with regards Brain tumors, one in six South African men and one in seven South African women will be diagnosed with cancer during their life times. Despite this small percentage, the diagnoses of brain tumors have escalated the last few years. The reason for these new statistics is still unknown.

With exercise that is becoming one of the most important adjuvant therapies for most diseases or illnesses, we may sustain this idea of using exercise intervention as an adjuvant therapy for brain tumor cancers we can prove this through many researches that has been done in the last few years. (Schwartz, 2003) Studies done by different researchers they found that exercise intervention is becoming increasingly recognized as a safe, feasible and beneficial supportive therapy for cancer patients both during and after the cessation of adjuvant therapy. (Jones *et al.*, 2006) Exercise influences a lot of different systems in the body, to the advantage of the cancer patient (Schwartz, 2003) and emerging new research shows that physical exercise may boost brain function, which include improve mood. (Kong, 1999) Exercise, according to Cotman and

Berchtold (2002) is commonly believed to be a behavioral strategy to relieve stress, and reduce depression and anxiety in humans. Exercise intervention further influence following aspects of the human body, namely brain deprived neurotrophic factor (BDNF) and 5-HT (Serotonin). Improvement of these could, in fact, lead to a better quality of life (QoL) of a brain tumor patient (Cotman & Berchtold, 2002).

Fatigue that sets in, due to the different cancer therapies, is also a factor that has an affect on depression and anxiety of the patient. Keeping still and rest to prevent fatigue were followed in previous regiment when working with cancer patients was followed. This approach, in fact, has a very negative effect on the patient. Being diagnosed with a brain tumor the patient will never be emotionally prepared for this type of information and it usually shatters their sense of well being and their personal security. All of these factors, especially depression, affect the patient's QoL. (Vaynman *et al.*, 2004)

An exercise regiment for brain tumor patients has not yet been developed properly, because exercise intervention for familiar cancers could be problematic and not suitable for brain tumor patients. (Schwartz, 2003) Therefore, the purpose of this study is to further the knowledge and the field of expertise of exercise as an adjuvant therapy in brain tumor patients to better QoL over a larger period of time.

Key words:

Brain tumor, prevalence, exercise intervention, adjuvant therapies, quality of life (QoL), brain deprived neurotrophic factor (BDNF), 5-HT (Serotonin), fatigue, depression, brain function.

OPSOMMING

| | |
|------------------|---|
| TITEL | 'n Dwarsdeursnee studie wat die oefeningsgedrag, voorkeure en lewenskwaliteit van primêre breingewas pasiënte ondersoek |
| KANDIDAAT | Adél Engelbrecht |
| PROMOTOR | Prof. P.E. Krúger |
| GRAAD | Magister Artium |

Die tweede grootste leier in siektes tussen die ouderdomme van 20-39 jaar wat lewens eis is Brein gewasse (brein kanker). (Armstrong *et al.*, 2004) Volgens die Suid-Afrikaanse Mediese Navorsingraad, is daar tot 801 gevalle van breingewas sterftes in die jaar 2000 aangemeld. As hierdie statistieke vergelyk word met statistieke van kanker wat meer prominent voorkom soos byvoorbeeld bors-, long-, en protaatkanker, lyk die voorkoms van breinkanker diagnosis maar na 'n baie klein persentasie. Die Mayo Kliniek in Suid-Afrika het in 2007 bevind dat die voorkoms van breinkanker in Suid-Afrika 'n persentasie van 3% uitgemaak het. Ten spyte van hierdie statistieke betreffende breingewasse, sal een uit elke ses mans en een uit elke sewe vroue, gediagnoseer word met een of ander kanker gedurende hulle leeftyd. Alhoewel die persentasie wat reeds genoem is maar na 'n klein hoeveelheid lyk, het die voorkoms van breingewasse baie toegeneem in die laaste paar jaar en selfs maande. Die rede vir hierdie aansienlike toename is steeds onbekend.

Oefening word al hoe belangriker en word al hoe meer deur verskeie dokters voorgeskryf om te dien as 'n bykomende behandeling vir verskeie siekte toestande. Dit word veral ook vir kanker pasiënte voorgeskryf. Oefen intervensie kan dus gebruik word vir breinkanker pasiënte, hierdie stelling gestaaf kan word, aangesien daar verskeie navorsings reeds bewys het dat oefening as bykomende terapie gebruik is vir kanker pasiënte. (Schwartz, 2003) Hierdie studies het bevind dat oefening as 'n veilige,

VII

uitvoerbare en voordelige bykomende intervensie vir kanker pasiënte erken word. Hierdie intervensie kan tydens en na hoof kanker behandeling gebruik word (Jones *et al.*, 2006).

Oefening beïnvloed verskeie sisteme in die liggaam, tot voordeel van die kanker pasiënt. (Schwartz, 2003) Nuwe navorsing het ook aan die lig laat kom dat fisieke aktiwiteit 'n persoon se breinfunksie bevorder, wat onder andere 'n baie groot invloed het om die pasiënt se gemoedstoestand. (Kong, 1999) Volgens, Cotman and Berchtold (2002), is daarvolgens studies bewys dat oefenterapie 'n manier is om stres te verlig, sowel as depressie en angstigtheid in meeste mense.

Oefenterapie beïnvloed ook die volgende aspekte positief in die menslike liggaam naamlik, Brein ontnemende neurtrofiese-faktor (BDNF) en 5-HT (Serotonien). Verbetering van hierdie faktore, kan ly tot 'n beter kwaliteit van lewe van 'n pasiënt wat met 'n breingewas gediagnoseer is (Cotman & Berchtold, 2002).

Uitputting (moegheid) wat gewoonlik intree as gevolg van kanker terapie, is ook 'n faktor wat 'n effek het op die depressie- en angsvlakke van 'n pasiënt. In vroeë behandelingsprotokol van kanker pasiënte, moes die pasiënt so stil as moontlik verkeer om sodoende uitputting of moegheid te voorkom. Hierdie benadering het in die uiteinde 'n baie negatiewe effek op die pasiënte tot gevolg gehad. 'n Persoon wat met 'n breingewas gediagnoseer word sal nooit emosioneel voorbereid wees op hierdie diagnose nie en sodoende kan dit lei tot 'n ineenstorting van die persoon se geestestoestand en persoonlike sekuriteit. Hierdie "ineenstorting" kan 'n groot invloed hê op die kwaliteit van lewe van hierdie pasiënt (Vaynman *et al.*, 2004).

'n Oefenterapie protokol vir breinkanker pasiënte is nog nie voldoende vasgestel nie, aangesien oefenterapie intervensies wat vir bekende kankers problematies en selfs gevaarlik kan wees vir breingewas pasiënte nie. (Schwartz, 2003)

Daarom is die doel van die studie, om inligting te verkry en kennis in te samel om die veld van deskundiges uit te brei om sodoende 'n oefenterapie protokol neer te lê vir

VIII

breinkanker pasiënte. Hierdie protokol sal dus dien as 'n bevordering van kwaliteit van lewe van hierdie pasiente deur middel van oefen intervensie as bykomende behandeling.

Sleutelterme:

Breingewas / breinkanker, voorkomssyfer, oefen intervensie, bykomende terapie, kwaliteit van lewe, brein ontnemende neutrofiese factor (BDNF), 5-HT (Serotonien), uitputting/moegheid, depressie, breinfunksie.

LIST OF TABLES

| | Page # |
|---|---------------|
| Table 1.1 The World Health Organization (WHO) has identified 4 grades of brain tumors (Armstrong <i>et al.</i> , 2004). | 2 |
| Table 2.1 The Basic TNM system identified four stages (Schneider <i>et al.</i> , 2003). | 17 |
| Table 2.2 Rehabilitation-related issues for Cancer Patients (Gerber, 2001). | 19 |
| Table 2.3 Affect of fatigue on cancer patient (Schneider <i>et al.</i> , 2003). | 26 |
| Table 2.4 Factors implicated in the pathogenesis of fatigue (Stasi <i>et al.</i> , 2003). | 31 |
| Table 2.5 Risk factors for Primary Brain Tumors (Chandana <i>et al.</i> , 2008). | 40 |
| Table 2.6 Focal neurologic signs and symptoms of Primary Brain Tumors (Chandana <i>et al.</i> , 2008). | 45 |
| Table 2.7 The Karnofsky Performance Scale (Crooks <i>et al.</i> , 1991). | 51 |
| Table 4.1 Results of responses on questions pertaining to Physical Well-being | 105 |
| Table 4.2 Results of responses on questions pertaining to Social/Family Well-being | 107 |
| Table 4.3 Results of responses on questions pertaining to Emotional Well-being | 108 |
| Table 4.4 Results of responses on questions pertaining to Functional Well-being | 109 |

| | | |
|------------|--|-----|
| Table 4.5 | Results of responses on questions pertaining to Fatigue | 111 |
| Table 4.6 | Results of responses on questions pertaining to Quality of Life | 112 |
| Table 4.7 | Results of responses on questions pertaining to Quality of Life (Continued) | 113 |
| Table 4.8 | Correlations between Indexes of Well-being | 119 |
| Table 4.9 | Perceptions of Exercise and how it will impact on their daily life and overall well-being | 131 |
| Table 4.10 | Perceptions of support and approval from others regarding exercise | 132 |

LIST OF FIGURES

| | Page # |
|-------------|--|
| Figure 2.1 | Different brain lobes and functions (Wikipedia, 2011). 42 |
| Figure 2.2 | Model to evaluate effects of different factors on brain tumor patients' overall quality of life (QoL) (Liu et al., 2008). 93 |
| Figure 4.1 | Marital statuses of questionnaire participants 102 |
| Figure 4.2 | Education of questionnaire participants 102 |
| Figure 4.3 | Employment status of questionnaire participants 103 |
| Figure 4.4 | Cigarette smoking habits of participants 104 |
| Figure 4.5 | Current smoking habits of participants 104 |
| Figure 4.6 | Participation in strenuous exercise by participants 121 |
| Figure 4.7 | Participation in moderate exercise by participants 123 |
| Figure 4.8 | Participation in mild exercise by participants 124 |
| Figure 4.9 | Necessity of receiving information about exercise programs 125 |
| Figure 4.10 | Participants that will participate in an exercise program 126 |
| Figure 4.11 | Preference of company to exercise with during illness 127 |
| Figure 4.12 | Preference of where to exercise 128 |
| Figure 4.13 | Preference of duration of exercise session/program 129 |
| Figure 4.14 | Preference of frequency of exercise program 130 |
| Figure 4.15 | Motivation of exercise participation 133 |
| Figure 4.16 | Confidence of patient to participate regularly in exercise sessions 134 |
| Figure 4.17 | Confidence of the patient's control over physical activity 135 |
| Figure 4.18 | Preference of through which media to be contacted with 136 |

OPERATIONAL DEFINITIONS OF CRITICAL TERMS

Adjuvant therapy: is treatment that is given in addition to the primary, main or initial treatment (Wikipedia, 2011)

Asthenia: lack or loss of strength and energy; weakness (The Free Dictionary by Farlex, 2008).

BDNF: Brain deprived neurotrophic factor is a protein that is crucial for the growth of neurons and for brain processes involved in learning and memory (Covalt, 2006).

Benign tumor: Slow growing tumor, which is in most cases curable and harmless. Mostly grade I and II by the World Health Organization (WHO) (Schneider *et al.*, 2003).

Blood brain barrier: a protective barrier formed by the blood vessels and glia of the brain. It prevents some substances in the blood from entering the brain (Segal, 1993).

Bone-morphogenetic protein (BMP): It is found throughout the body, affects cellular development in various ways, some of them deleterious. In the brain BMP has been found to contribute to the control of stem cell divisions (Reynolds, 2010).

Carcinogen: Substance that causes cancer (Armstrong *et al.*, 2004).

Cancer related-fatigue (CRF): a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer-related treatment that is not proportional to recent activity and interferes with usual functioning (Velthuis *et al.*, 2009).

XIII

Cancer survivor or survivorship: span from day of diagnosis till the day of death. So this means remaining a survivor of this disease until the moment of death (Seyama & Kanda., 2010).

Central nervous system: consists of the brain and the spinal cord (Purchon, 2006).

Cerebral blood flow: The flow of the blood through the brain, important for delivery of oxygen and removal of “waste” products (Walters, 1998).

Cerebral perfusion pressure: The effective pressure driving blood through the brain (Walters, 1998).

Cerebral Tumor: A tumor arising within the skull (Brown *et al.*, 2006).

Chemotherapy: the use of chemical agents to treat brain tumors, it inhibits cell division which in resulting in diminished production of new cells (Armstrong *et al.*, 2004).

Choroid plexus: Choroid plexus of the blood vessels, which three lies in the brain, one in each lateral ventricle and one in the third ventricle. They secrete the cerebrospinal fluid (Brown *et al.*, 2006).

Dopamine: One of the catecholamine neurotransmitters in the brain. It is derived from tyrosine and is the precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain; and important in regulating movement (Medical Dictionary Online, 2006).

Edema: Swelling due to an excess of water (ABTA’s Dictionary for Brain tumor patients, 2005).

Exercise intervention: Certain exercise protocol being used to reach certain criteria in this study.

XIV

Focal deficit: Damage to sensory or movement abilities, problems in the ability to process information, personality changes, and speech disorders (Armstrong *et al.*, 2004).

Focal seizures: Slight and quick-muscle or eye twitching, or a sense of being “out of the moment” mentally and/or physically for a brief time; a blank stare or sudden pause without response (Roberts & Musella, 2005).

Glioma: Any tumor arising from glial tissue. Different kinds of glioma may be diagnosed due to the anatomy it affects (Armstrong *et al.*, 2004).

Glioblastoma Multiforme: The most common malignant primary brain tumor in adults. A grade IV tumor according to the World Health Organization (WHO) (Levin *et al.*, 2006).

Glucocorticosteroids: Medication used to decrease swelling around tumor (Adlard & Cotman, 2003).

Grade of brain tumor: Specific classification that relates to the current speed of growth and the potential interfere with brain function (Roberts & Musella, 2005).

Grand mall seizures: It involves the whole body activity with a seizure (Roberts & Musella, 2005).

Hippocampus: A curved elevation of gray matter extending the entire length of the floor of the temporal horn of the lateral ventricle (Medical Dictionary Online, 2006).

Hypophysis: Pituitary gland (Armstrong *et al.*, 2004).

Hydrocephalus: An abnormal amount of fluid, called cerebrospinal fluid in the brain that causes brain swelling. The fluid is usually absorbed by the 3 layers of membranes of the brain into the bloodstream (Brown *et al.*, 2006).

Immunotherapy: The block of cancer-cell receptors for growth-stimulating factors, but can cause several symptoms (American Cancer Society, 2011).

Intracranial pressure: The pressure within the rigid skull (Walters, 1998).

Malignant tumors: These are the aggressive type, problematic to operate on and are still in these days incurable. They are considered fast growing, rapidly invading nearby tissue. It could either be a grade III and IV by the WHO (Armstrong *et al.*, 2004).

Medulla: It is the Latin word for “marrow”, the inner or middle part of a structure of organ (Wikipedia, 2011).

Metastatic brain tumor: A brain tumor caused by cancer elsewhere spreading to the brain (Segal, 1993).

Melanocytes: Malignant pigment-producing cells in the skin (Schneider *et al.*, 2003).

MIB-I labeling index: The index that measures the percentage of cells that are actively dividing within the tumor (Armstrong *et al.*, 2004).

MRI scan: Magnetic Resonance Imaging. MRI is a scanning device that uses a magnetic field, radio computer. Signals emitted by normal and diseased tissue during the scan are assembled into an image (Armstrong *et al.*, 2004).

Necrosis: Death of cell or tissue due to injury or disease, especially in a localized area of the body (The Free Dictionary by Farlex, 2001).

Neoplasm: New growth (Schneider *et al.*, 2003).

Noggin: A brain protein that acts as a BMP (Bone Morphogenetic Protein) antagonist (Reynolds, 2010).

Pinocytosis: Introduction of fluids into a cell by invagination of the cell membrane (The Free Dictionary by Farlex, 2001).

Pons: Part of the brain stem that lies in front of the cerebellum and below the cerebral hemispheres (Brown, 2006).

Primary brain tumor: Cancerous growth that originates in the brain (Jones *et al.*, 2006).

Prognosis: A forecast of a probable course and outcome of an illness or a prediction of the course of a disease (eLook Online Dictionary, 2011).

Radiation therapy: The use of radiation energy to interfere with tumor growth irradiation (Brown, 2006).

Serotonin (5HT): A biochemical messenger and regulator, synthesized from the essential amino acid L-Tryptophan (Anon, 2007).

Tryptophan: An essential amino acid (building block of protein) that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor of serotonin (Helmenstine, 2007).

Seizure, Convulsions, Epilepsy: sudden and abnormal electrical activity in the brain (Segal, 1993).

XVII

Tumor: An abnormal mass of tissue that results when cells divide more than they should or do not die when they should (National Cancer Institute, 2006).

WHO: World Health Organization (Meyers & Hess, 2003).

5-HIAA: 5-hydroxyindoleacetic acid (5-HIAA) -- a break-down product of the chemical messenger serotonin -- in urine (Discovery Fit & Health, 2007).

INDEX

| | Page # |
|---|--------|
| ACKNOWLEDGEMENTS | III |
| SYNOPSIS | IV |
| OPSOMMING | VI |
| LIST OF TABLES | IX |
| LIST OF FIGURES | XI |
| OPERATIONAL DEFINITIONS OF CRITICAL TERMS | XII |

CHAPTER 1

INTRODUCTION

| | | |
|-------|---|----|
| 1.1 | Introduction | 1 |
| 1.2 | Research problem | 6 |
| 1.3 | Research hypotheses | 6 |
| 1.4 | Assumptions, Delimitations and Limitations of the study | 7 |
| 1.5 | Type of study | 7 |
| 1.6 | Study Population | 8 |
| 1.6.1 | Inclusion criteria | 8 |
| 1.6.2 | Exclusion criteria | 8 |
| 1.7 | Study sample | 8 |
| 1.8 | Research design | 8 |
| 1.9 | Dependant variables | 9 |
| 1.10 | Independent variables | 9 |
| 1.11 | Data collecting procedures | 9 |
| 1.12 | Clinical value | 10 |
| 1.13 | Anticipated problems | 10 |
| 1.14 | Statistical tools | 10 |
| 1.15 | Goal | 11 |
| 1.16 | Objectives | 11 |

CHAPTER 2

LITERATURE REVIEW

| | | |
|---------|---|----|
| 2.1 | Cancer | 12 |
| 2.1.1 | How cancer develops | 12 |
| 2.1.2 | Types of Cancer | 15 |
| 2.1.3 | Grading and Staging of Tumors | 16 |
| 2.2 | Cancer Treatment and the Effects on Physiological systems | 17 |
| 2.2.1 | Fatigue | 20 |
| 2.2.1.1 | What is fatigue? | 20 |
| 2.2.1.2 | Pharmacological and Non-Pharmacological treatment of CRF | 22 |
| 2.2.1.3 | Prevalence of fatigue | 23 |
| 2.2.1.4 | Cancer treatment and fatigue | 24 |
| 2.2.1.5 | Different perceptions of fatigue | 25 |
| 2.2.1.6 | Exercise vs. resting and fatigue | 27 |
| 2.3 | Exercise Fundamentals and Cancer Patients | 32 |
| 2.3.1 | Physiological adaptation of Cancer patients to Exercise | 34 |
| 2.4 | What is a Brain Tumor? | 36 |
| 2.4.1 | Classification of Brain Tumors | 37 |
| 2.4.1.1 | Primary Brain Tumors and possible causes | 37 |
| 2.4.2 | How to understand the Brain | 40 |
| 2.4.2.1 | Spinal cord | 41 |
| 2.4.2.2 | Cerebrum | 41 |
| 2.4.2.3 | Thalamus | 43 |
| 2.4.2.4 | Hypothalamus | 43 |
| 2.4.2.5 | Pituitary Gland | 43 |
| 2.4.2.6 | Brain stem | 43 |
| 2.4.2.7 | Cerebellum | 44 |

| | | |
|--------|--|----|
| 2.5 | The Diagnosing and Symptoms of the Brain Tumor | 44 |
| 2.5.1 | Symptoms of a Brain Tumor | 44 |
| 2.5.2 | Diagnosing of a Brain Tumor | 46 |
| 2.5.3 | Analysis of the Brain Tumor tissue | 47 |
| 2.5.4 | Tumor origination | 48 |
| 2.5.5 | Location of the Brain Tumor and adjustment of the Patient | 49 |
| 2.5.6 | Pre-treatment assessment of the Patient | 50 |
| 2.6 | Different types of Primary Brain Tumors | 51 |
| 2.6.1 | Glial tumors | 52 |
| 2.6.2 | Non-glial tumors | 53 |
| 2.7 | Treatment of Brain Tumors and the Effects on the Patient | 54 |
| 2.8 | Quality of life and the Brain Tumor Patient | 57 |
| 2.9 | Occurrence and Prognosis of Primary Brain Tumors | 58 |
| 2.10 | Statistics of Brain Tumors | 60 |
| 2.11 | Exercise intervention and the Human Brain | 61 |
| 2.11.1 | Processes in the Brain during Exercise | 61 |
| 2.11.2 | Mind-Body connection through Exercise | 62 |
| 2.11.3 | Neurogenesis and Exercise | 63 |
| 2.11.4 | Exercise-releasing natural chemicals that enhance Brain health | 64 |
| 2.12 | Exercise, the Brain and different systems | 66 |
| 2.12.1 | Chemical regulators | 66 |
| 2.12.2 | Brain Deprived Neurotrophic Factor (BDNF) | 67 |
| 2.12.3 | Cerebrospinal Fluid (CBF) and Serotonin (5HT) | 68 |
| 2.12.4 | Blood-Brain Barrier (BBB) | 70 |
| 2.12.5 | Cardiorespiratory component and the Brain | 71 |

| | | |
|----------|--|----|
| 2.13 | Exercise Intervention and the Brain Tumor Patient | 72 |
| 2.13.1 | Cancer-related Fatigue and the Brain Tumor Patient | 74 |
| 2.13.2 | Influence of Exercise Intervention on Cancer-Related symptoms including cancer-related fatigue | 75 |
| 2.13.3 | Symptoms and intervention that influence ADL of Primary Brain Tumor patient | 76 |
| 2.14 | Exercise Intervention for high risk or chronic illnesses | 77 |
| 2.15 | Exercise recommendation for Brain Tumor Patients | 78 |
| 2.15.1 | Positive influence of exercise on Brain Tumor Patients | 78 |
| 2.15.2 | Exercise recommendation during cancer treatment for Brain Tumor Patients | 79 |
| 2.15.3 | Type and Duration of Exercise Intervention prescription | 81 |
| 2.15.4 | Cardiovascular component of Exercise Intervention | 84 |
| 2.15.5 | Intensity of Exercise Intervention | 85 |
| 2.15.6 | Exercise termination | 85 |
| 2.16 | Holistic approach in Exercise prescription for the Brain Tumor Patient | 86 |
| 2.17 | Factors for concern surrounding Exercise Intervention | 88 |
| 2.18 | Primary Brain Tumor and care of the Patient | 88 |
| 2.18.1 | The Brain Tumor Patient and Management with the prognosis | 89 |
| 2.18.1.1 | The Caregiver, the Patient and QoL | 90 |
| 2.18.1.2 | The Caregiver, the Patient and ADL | 93 |
| 2.18.1.3 | The Caregiver, the Patient and exercise | 95 |
| 2.19 | Research on management programs for Brain Tumor Patients and their families | 95 |

CHAPTER 3

METHODOLOGY

| | | |
|-------|------------------------|----|
| 3.1 | Objectives | 97 |
| 3.2 | Methodology | 97 |
| 3.3 | Statistical analysis | 98 |
| 3.3.1 | Descriptive statistics | 98 |
| 3.3.2 | Inferential statistics | 98 |

CHAPTER 4

RESULTS AND DISCUSSION

| | | |
|-------|---|-----|
| 4.1 | Results | 101 |
| 4.2 | Description of the sample | 101 |
| 4.3.1 | Results of the analysis of indexes: Physiological, Social, Emotional, Functional Well-being, fatigue and QoL | 105 |
| 4.3.2 | Results of Patients' Responses to the Questions Pertaining to the Indexes of Physical, Social, Emotional and Functional Well-being, Fatigue and Quality of Life | 105 |
| 4.3.3 | Results of the Correlation Analysis between the Indexes of Physical, Social, Emotional and Functional Well-being and Fatigue and Quality of Life | 116 |
| 4.3.4 | Results of the Analysis of Statistically Significant Differences between Patients who Exercised versus those who did not on all Index Scores | 120 |

| | | |
|------------|--|------------|
| 4.3.5 | Results of the Analysis of Patients' Participation in Sport and Exercise Preferences | 121 |
| 4.3.6 | Results of the Analysis of Patients' Beliefs regarding Exercise and their intention of exercise in coming months | 131 |
| 4.3.7 | Patients' Preferences Regarding the Media they prefer for Receiving Information Regarding Exercise Programs | 136 |
| 4.4 | SUMMARY OF RESULTS | 137 |
| 4.5 | DISCUSSION OF RESULTS | 138 |
| <hr/> | | |
| | CHAPTER 5 | |
| | SUMMARY, CONCLUSION AND RECOMMENDATIONS | 141 |
| <hr/> | | |
| | BIBLIOGRAPHY | 149 |

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

Cancer is one of the most feared diseases of our time; because anybody could become a victim of this disease due to the different ways it could develop or affect the person. Cancer is one of the most researched diseases of all times, and still the ways of treatment of it will change daily or monthly, due to physiological differences of patients and different types and grades of cancers.

Cancer is not a single disease; it is a collection of hundreds of diseases that share the common feature of excessive, uncontrolled cellular proliferation and the potential for these cells to spread to distant anatomical sites are great (Schwartz, 2003). Cancer that originates at one anatomical site will usually be diagnosed as the primary cancer site. If this cancer is not treated or diagnosed early, it will spread to a distant anatomical site and this is called a metastasis.

The fear of the disease of cancer is that it is a life threatening, which if it is not treated accordingly, it will in the end take the patient's life. Some researchers argued that brain tumors are not cancer, due to the fact that it rarely spread outside the brain. On the other hand, brain tumors are life threatening, and therefore could be classified as a cancer (Roberts & Musella, 2005). All tumors are given a certain grade or classification and these grades will provide the oncologist or other doctors that is part of the treatment the information they need for the treatment and what the patient can expect (see Table 1.1).

The classification of the tumor relates to the current speed of growth and potential interference with brain functioning (Roberts & Musella, 2005).

Table 1.1: The World Health Organization (WHO) has identified 4 grades of brain tumors (Armstrong *et al.*, 2004).

| GRADE | NAME | STATUS |
|-------|-------------------------|-----------|
| I | Pilocytic Astrocytoma | Benign |
| II | Low grade Astrocytoma | Benign |
| III | Anaplastic Astrocytoma | Malignant |
| IV | Glioblastoma Multiforme | Malignant |

Benign tumors are not considered cancer. They are slow growing and can be destroyed or removed if it is in an accessible area (National Brain Tumor Society, 2011). The problem with the slow growing of this tumor and the onset of the tumor is often insidious and only gradually comes to the attention of the patient before they experience any symptoms (Bederson, 2008 *In*: Charles, 2008). In the above table it shows that Grade I and II tumors are listed as benign tumors. The WHO sometimes list these two grades under Grade I, then Grade III and IV will be listed one grade down, e.g. Grade III will become grade II (Armstrong *et al.*, 2004).

Malignant tumors are tumors that are very different in appearance and highly unorganized compared to normal brain cells. These tumors are of the aggressive type, problematic to operate on and hard to cure (American Brain Tumor Association, 2011). Grade III and IV will be classified under malignant tumors. High-grade gliomas are extremely aggressive tumors (Brown *et al.*, 2006). The dangers of all grades of brain tumors, is that all cases the growth is limited to the enclosed area of the skull. Therefore, the chances of it affecting brain function due to intercranial pressure, even if it is classified as benign, could be hazardous to the patient and could even lead to death (Roberts & Musella, 2005).

Cancer is feared to be one of the major killers throughout both the development and developing world, including South Africa, according to the National Cancer Registry

(NCR). The burden of Cancer over the last 30 years has dramatically increased and it was estimated in 2008 that 12 million new cases of cancer diagnosed, 7 million deaths from cancer and 25 million persons living with cancer. According to the NCR's estimates, Cancer will be the leading cause of death globally in the year 2010 (Thom, 2008).

According to Peter Boyle, the IARC director, predicts in 2008 that by 2030 there will be 27 million cases of cancer, 17 million cancer deaths annually and 75 million persons living with cancer within 5 years of diagnosis. (Boyle, 2008 In: Thom, 2008).

One in six South African men and one in seven South African women will be diagnosed with cancer during their lifetimes. According to the Mayo Clinic in South Africa, the estimate number of brain tumor incidences was 3% in 2007 (www.mayoclinic.co.za). In the United States of America an estimated 50 adults will be diagnosed with a primary brain tumor every day. Brain tumors are the second leading cause of cancer death in young adults aged 20 – 39 years (Armstrong *et al.*, 2004). According to the South African Medical Research Council, there was an estimate 801 deaths because of brain cancer in South Africa in 2000. If these statistics are compared to other types of cancers like breast-, lung- and prostate cancers, is the prevalence of the diagnoses of brain tumors, a very small percentage. Despite this small percentage, the diagnoses of brain tumors have escalated the last few years. The reason for these new statistics is still unknown at this time.

Brain cancer presents an almost fourfold variation in incidence around the world. According to the brain cancer incidence rate by regions of the world, South Africa 1.2 rate/100 000 ASR world population done in 2002, South Australia has the highest number of 5.3 rate/100 000 ASR world populations. The variation between countries over the world is also unknown (Cancer Council South Australia, 2006).

Exercise intervention is becoming increasingly recognized as a safe, feasible and beneficial supportive therapy for cancer patients both during and after the cessation of

adjuvant therapy (Jones *et al.*, 2006). The adjuvant therapies include surgery, chemotherapy, radiation therapy and immuno-therapy. These therapies are the standard procedures that a brain tumor patient will receive. The goals of exercise intervention therapy may differ depending on whether a patient is receiving initial treatment for a new diagnosis, is in remission or is receiving treatment for a recurrence (Schwartz, 2003).

The idea of using exercise intervention as an adjuvant therapy for brain tumor cancers can be proved by many research that has been done in the last few years. Exercise may influence a lot of different systems in the body, to the advantage to the cancer patients (Schwartz, 2003). It is further possible that some of the beneficial aspects of exercise act directly on the molecular machinery of the brain itself, rather than on the general health. Several molecular systems could potentially participate in the benefits of exercise on the brain. These data from humans are supported by animal research demonstrating that exercise and/or behavioral enrichment can increase neuronal survival and resistance to brain insult, promote brain vascularization, stimulate neurogenesis, enhance learning and contribute to maintenance of cognitive function during aging (Cotman & Berchtold, 2002). Emerging new research shows that physical exercise may boost brain function, which include improve mood, and otherwise increase learning ability (Kong, 1999).

Exercise is also commonly believe to be a behavioral strategy to relieve stress, and can reduce depression and anxiety in humans (Cotman & Berchtold, 2002). Exercise intervention further has an influence on the following aspect of the human body, namely increased level of *Brain Deprived Neurotrophic Factor* (BDNF), which is a protein that is crucial for the growth of neurons and for brain processes involved in learning and memory (Cotman & Berchtold, 2002). It is also crucial for the synthesis of Serotonin (5HT) in the hippocampus and helps better the neurotransmission in the brain (Garza *et al.*, 2003). Improvement of the above-mentioned states, could in fact lead to a better quality of life (QoL) of the brain tumor patient.

Due to the life changes that the brain tumor patient experience during diagnosis and the time thereafter, the patient will often experience different sorts of discomfort, because all patients' reaction to therapy is unique and must be discussed with his or her doctor or oncologist to help alleviate these discomforts (Armstrong *et al.*, 2004).

Fatigue that sets in, due to the different therapies, is also a factor that has an effect on depression and anxiety of the patient. According to a statement made by Vaynman *et al.* (2004), the patient diagnosed with a brain tumor will never be emotionally prepared for this type of information and it usually shatters their sense of well-being and their personal security. All of these factors, especially fatigue and depression, affect the patient's QoL.

Fatigue formed the basis of following a regiment of exercise intervention started by researchers like Dr. Lee W. Jones at Duke University in North Carolina in the United States. Fatigue has a very negative effect on the patient. Fatigue is most common complaint among any cancer patient. Coming from a very conservative approach to the treatment of cancer patients to adjuvant treatment like exercise intervention that Dr. Jones and colleagues started on breast cancer patients. This treatment to lessen the fatigue levels will differ for different types of cancers though, but it did show that there where positive behavioral change in patients and brain tumor patients where very interested and motivated to be exposed to exercise intervention (Jones *et al.*, 2006).

Research in the practice of exercise oncology or intervention in the South Africa, has mostly been on familiar types of cancers. The research on this regiment or adjuvant therapy for primary brain tumor patients must be researched because; it has not yet been developed properly, and it must then be incorporated as soon as possible and it must be specified for brain tumor patients only. Exercise interventions for familiar cancers could be problematic and not be suitable for brain tumor patients (Schwartz, 2003). The reason for this is that the idea for a cancer patient to keep still and rest throughout the treatment regimen was followed. A brain tumor patient was thought to be a hazardous area to tread on if you are an Exercise Specialist.

The purpose of this study is to further the knowledge and the field of expertise of exercise as an adjuvant therapy in brain tumor patients to better their QoL over a longer period of time.

1.2 RESEARCH PROBLEM

According to numerous studies, exercise has a positive influence on the decreasing in fatigue levels of cancer patients. In conjunction with these literatures, the influence of exercise on brain tumor patients could also have a positive effect on certain outcomes on the health status of these patients. Brain tumor patient's quality of life (QoL) is foremost number one, thinking on initiating an exercise protocol for this population (Jones *et al.*, 2006). Brain Cancer patients' life expectancy could be brief according to Brown *et al.* (2006), and therefore it is important for the patients' as well as for their caregivers, that the patient has QoL for as long as possible.

This population of patients tends to fall into a pattern of severe depression after they have been diagnosed as well as through periods of their treatment. This is why it is important that the patient is relieved from as much unnecessary stress factors as possible. Cotman *et al.* (2007) showed that exercise is a behavioral strategy to relieve stress, and that it can reduce depression and anxiety in humans.

Therefore, it is important to ask the following question:

- Will different exercise behavior have an effect on quality of life in primary brain tumor patients?

1.3 RESEARCH HYPOTHESIS

In the study among primary brain tumor patients the following hypotheses will be studied:

- Will different exercise preference have a different impact on the quality of life of brain tumor patients; and

- Will different exercise behavior have a different impact on the quality of life of brain tumor patients;

1.4 ASSUMPTIONS, DELIMITATIONS AND LIMITATIONS OF THE STUDY

1.4.1 Assumptions

The following assumption will be made:

- It will be assumed that patients that has been diagnosed and recruited for this study are willing to participate in this study by completing the necessary questionnaires; and
- It will be assumed that the questionnaires used to measure outcomes are valid and reliable.

1.4.2 Delimitations

The study will focus on exercise behavior and –preference and its effect on the quality of life of the primary brain tumor patients.

1.4.3 Limitations of study

This study is only for patients being diagnosed with a primary brain tumors and not any other brain deficiency like chronic headaches, Alzheimer's or Parkinson's disease.

1.5 TYPE OF STUDY

- The scope of the research undertaken is thus delimited to a cross-sectional study;
- The cross-section study will apply, where this will be descriptive study of brain tumor patients' exercise behavior; and
- These patients will complete the 2 questionnaires that will be establishing their exercise behavior before, during and after treatment.

1.6 STUDY POPULATION

This study will include subjects, both male and female, that have been diagnosed with a primary brain tumor. This will include any stage of diagnosis, including before treatment, during treatment as well as patients with a recurrence.

1.6.1 Inclusion criteria

- Patients that were diagnosed with a primary brain tumor by use of a Magnetic Resonance Imaging (MRI), a CAT scan and/or a biopsy, which will specify what type of tumor and area of the brain is affected. The area of the brain will determine the patient's neurological deficit.
- Patients must be under the treatment of an oncologist.

1.6.2 Exclusion criteria

- Patients with a metastatic brain tumor; and
- Patients with a lower grade brain tumor, because it is a total different disease than a higher-grade brain tumor.

1.7 STUDY SAMPLES

Subjects or potential patients will be recruited through the oncology practices and then approached directly or by postal service to provide them with the necessary information of the study, and will be asked if they were willing to participate in the study. If they do they will complete the two questionnaires, namely the FACT-Br and the Quality of life (QoL) questionnaires. The recruited patients will remain under the supervision of an oncologist.

1.8 RESEARCH DESIGN

The design of the study will be a cross-sectional study. Cross-section studies give us the opportunity to study a disease and exposure status are measured or studied simultaneously in a certain population. This study will give us an indication behavior in exercise among primary brain tumor patients. The questionnaires, and literature

supporting this study, we will determine if this exercise behavior have a positive influence on the quality of life of primary brain tumor patients.

The aim of this a cross-sectional study design, is to recruit and identify as many as possible patients diagnosed with a primary brain tumor in the last 12 months and they will have to complete the Functional Assessment of Cancer-Therapy-Brain scale (FACT-Br) questionnaire and Quality of Life questionnaire.

1.9 DEPENDENT VARIABLES

The main purpose of this study is to evaluate exercise preferences and exercise behavior on the following dependent variables of brain tumor patients: the Quality of Life of the primary brain tumor patient by assessing the patients physical well-being, social/family well-being, emotional well-being, functional well-being as well as additional concerns which are associated with brain tumor patients only.

1.10 INDEPENDENT VARIABLES

Think of an experiment as a cause-and-effect proposition, the cause is the independent variable and the effect is the dependant variable. Therefore, the independent variables are the different exercise preferences and the different exercise behaviors, while the dependent variables are the performance status, physical well-being, social/family well-being, emotional well-being, and functional well-being. The independent variable in this case, with brain tumor patients, will therefore be the type of exercises and exercise preferences and the effect that this will have on their overall well-being.

1.11 DATA COLLECTING PROCEDURES

Data will be collected through the completing of two questionnaires, namely: the FACT-Br and the Quality of Life-questionnaire. Data will also be collected through literature study of previous documentation of these types of studies on brain cancer patients or studies been done on cancer patients.

1.12 CLINICAL VALUE

This research study will provide an understanding of if exercise preferences and exercise behavior may help a patient living with a brain tumor to maintain a certain level of quality of life during their time of illness. Exercise could influence patients' overall well-being. This study could give a new way of treatment for brain tumor patients and give hope of handling the illness in a different way.

1.13 ANTICIPATED PROBLEMS

The recruiting enough patients for this study could be a problem. It would probably be a problem to get enough returning response from these patients that had to complete the questionnaires.

1.14 STATISTICAL TOOLS

The collected measurements were captured on a computer and analyzed by means of the SPSS package (Statistical Product and Service Solutions). The following statistical techniques were used to do the analysis.

- Spearman rank-order correlations: Spearman's rho will be used to determine the correlations between Physical, Social, Emotional, and Functional Well-being and perceptions of Fatigue and Quality of Life. Spearman's rho is a non-parametric version of the Pearson correlation coefficient, based on the ranks of the data rather than the actual values.
- The Mann-Whitney Test: The Mann-Whitney test will be used for testing differences between means when there are two conditions and different subjects have been used in each condition. This test is a distribution-free alternative to the independent samples t-test. Like the t-test, Mann-Whitney tests the null hypothesis that two independent samples (groups) come from the same population (not just populations with the same mean).

1.15 GOAL

The goal for this study is to investigate and anticipate the exercise preference of a brain cancer patient and the quality it might have on their daily activities. An exercise intervention program could then be implemented in the near future, that will be handled by the medical staff or the caregiver who will be working or caring for the primary brain cancer patient to provide a adjuvant therapy and to better the patient's quality of life over a longer time span of his/her life.

1.16 OBJECTIVES

The study aims to achieve the goal through its objectives, which are:

- To build a theoretical and practical frame of reference on exercise program for medical staff (e.g. Biokineticists or Physiotherapists) and caregivers. Early detection of this disease's exercise intervention program will differ from the program of a late detection. The role of the medical staff, as well as the caregivers will change the longer the patient is under medical treatment of chemotherapy and radiotherapy.
- To do a need assessment to understand the patients' needs and expectations of the exercise intervention program for medical staff and caregivers.
- To do a need assessment to understand caregivers' and patients' needs and expectations of the exercise intervention program.
- To develop the exercise intervention program while taking into account the literature study, previous exercise intervention programs for Cancer patients and the knowledge gained from the need assessments of the patients and the caregivers.
- To implement the exercise intervention program on the medical front and with caregivers.
- To evaluate the impact of the exercise intervention program on the patients and caregivers.
- To come to conclusions and recommendations regarding the dissemination of the program.

CHAPTER 2

LITERATURE STUDY

2.1 CANCER

Cancer is a general term for an abnormal growth of cells (Ko *et al.*, 2002). Cancer is a common diagnosis and often a chronic and complex disease (Gerber, 2001). According to the Pears Pocket Medical Dictionary, it states that Cancer is a malignant tumor. This so called tumor are cells which multiply in a disorderly and uncontrolled way, that invade surrounding tissue, and can give rise to secondary growths in parts of the body remote from the original tumor (Brown, 2006). Cancer can also be described as the uncontrolled proliferation of one or more cell populations interferes with normal biological functioning and therefore, this uncontrolled cell proliferation is called “hallmark of cancer” (Sherr, 1996; O’Conner & Browder, 1998).

Although cancer is not always malignant and can be benign, this is slow growing but become very large. Therefore it is stated that rapid cell growth is not always malignant (Ko *et al.*, 2002). Cancer cells are very well organized and well differentiated, and they do not have the destructive potential of malignant tumors. Benign tumors can damage adjacent areas and experience some areas of necrosis, but they rarely cause death (Schneider *et al.*, 2003). Despite all these physiological explanation of this disease, the person that is diagnosed with cancer usually will see it an incredible disturbing disease and sometimes a death sentence. The physiology of cancer could be very complicated to explain to a patient, but still therefore it important to let the patient understand why and how this disease develop and they can deal with it to the best of their ability.

2.1.1 How cancer develops

We have a million different types of cells that grow, function, form and differentiate every day. All of these different cells contain pairs of chromosomes. Deoxyribonucleic acid (DNA) molecules or genes spiral throughout each pair of chromosomes, giving the cell the “blueprint for life” (Schneider *et al.*, 2003). Global transcriptional analyses have

demonstrated that gene expression patterns greatly vary depending on cells history (Daignan-Fornier & Sagot, 2011).

The genes are sending the messages through to the different cells to either grow or function etc. Our chromosomes contain millions of different genes, pieces of DNA containing information on how these cells should function properly (Ko *et al.*, 2002). In most cases these messages that is transmitted by the genes or the DNA, are correct, but sometimes “mistakes” do occur and during reproduction mutations can develop in one or more of these cell’s genes. Since the chromosomes reproduce themselves every time a cell divides, there are lots of opportunities for something to go wrong (Ko *et al.*, 2002). Our body although do have the ability to correct these “mistakes”, but in some cases these genetic change results in an abnormal chromosome within the cancer cell (Schneider *et al.*, 2003). Different cells behave differently, as can be seen in the study by Daignan-Fornier and Sagot (2011), and cells may go into a quiescence stage. Quiescence is the most common cellular state on earth. While it is relatively easy to describe a proliferating cell, defining a quiescent cell is rather difficult. The only way to best describe a quiescence cell is a “reversible absence of proliferation” (Daignan-Fornier & Sagot, 2011). This means if the cell growth is reversible; it will depend on how it will proliferate and how the gene expression will express itself in this growing phase.

The next questions are then are how normal cells become cancerous and when does this “mistakes” in the chromosomes happen? Cancer results from genetic change or damage to a chromosome within a cell (Ko *et al.*, 2002), but there is no doubt that acquired mutations in individual genes (DNA) play a critical role in cancer, but according to Hunter it cannot be looked at in isolation though (Steeg *et al.*, 2009).

Carcinogenesis, which is one cause, is defined as the process by which a normal cell becomes cancerous. We grow throughout a significant sixteen years of our lives. The memory of a set of genes tells the cell at some point to “switch off”. This means at some point we will stop growing. Normal cells “obey the rules”, but cancer cells do not. The

change in the genetic code in the gene of the cancer cell erases its memory to “stop dividing” (Ko *et al.*, 2002).

Cancer starts with one abnormal cell (Ko *et al.*, 2002). This process happens in two stages Initiation and promotion with a number of sub stages, which Schneider *et al.* (2003) shows in their book “Exercise and Cancer recovery”, which I will include in this study for explanation. In the *pre-initiation* period, the genetic components of the chromosomes are protected from the effects of carcinogens. The attack or assault of the carcinogen on the genome of the cell happens in the first stage (initiation). Either the cell’s DNA is *altered by direct damaged to the DNA molecules, or the cell’s DNA repair system becomes inhibited and repair cannot occur. The second phase or *promotion* begins when the gene is expressed within the cell. This is when the cell begins to uncontrollable division and tumor promotion. This genetic information of this mutation of the cell can be expressed or repressed. Internal or external factors influence whether a mutated gene will be expressed or repressed (as recorded by De Vita *et al.*, (1997) and Snyder (1986) in Schneider *et al.*, 2003). Genetic background does have an influence on cancer development. *Polymorphisms* - DNA sequence differences among individuals - account for variations in many normal physiological traits and also accounts for different gene expression and variations in primary tumors from a variety of tissues (Steeg *et al.*, 2009).

Cancer is a chronic disease that is caused by defective genome-surveillance and signal-transduction mechanism. If infection and inflammation enhance tumor development, they must do so through signal-transduction mechanisms that influence factors involved in either malignant conversion or cancer surveillance (Karin, 2006). The functional relationship between inflammation and cancer is not new. In 1863, Virchow hypothesized that the origin of cancer was at sites of chronic inflammation and this type of chronic inflammation enhance cell proliferation (Coussens & Werb, 2002).

To understand the role of inflammation in the evolution of cancer, it is important to know how inflammation contributes to the physiological and pathological systems of the body,

including wound healing. We know that wound healing has to do with release of leukocytes or white blood cells, which will be directed to the sites of damage. The key concept is that normal inflammation for example, inflammation associated with wound healing is usually self-limiting; however, dysregulation of any of the converging factors can lead to abnormalities and ultimately, pathogenesis (Coussens & Werb, 2002).

The real reason of cancer development has gained popularity over a very long period of time. The cause of cancer will always be speculation and researchers will find a carcinogen that may cause cancer, but in most cases these studies will end up to be inconclusive. The researchers call it “hits”. The number of hits, the types of hits, the frequency of hits, and the intensity of the hits are critical to the development of cancer. (Schneider *et al.*, 2003)

2.1.2 Types of cancers

The Cancer or the Tumors are named according to the tissue it originates in and the degree of differentiation. There are 5 broad types of cancer in the Human Body:

1. Carcinomas are solid tumors that originate in the epithelial cells (lining of all tissue). The carcinomas may occur in the lungs, breasts, uterus, kidneys, esophagus, stomach and the intestinal tract (Schneider *et al.*, 2003).
2. Melanomas are malignant tumors of the melanocytes. Melanocytes are cells that produce the dark pigment, melanin, which are responsible for color of skin. They are found throughout the body and mainly occur in the skin, but may occur in the bowel and the eyes (Wikipedia, 2011).
3. Sarcomas are a type of cancer that forms from tissue like bone and muscle. Usually connective tissue or tissue that gives structure. Soft-tissue sarcomas develop in fat, blood vessels, nerves, muscles, fibrous tissue and deep skin tissue. Bone sarcomas only forms in the bones (American Cancer Society, 2010).
4. Leukemia is cancer of blood-forming organs that results from abnormal white blood cell (Leukocyte) production in the bone marrow (Brown *et. al.*, 2006).

5. Lymphoma is cancer of the white blood cells (WBC) or the lymphocytes. This usually causes the lymph glands and other organs where lymphocytes develop to enlarge due to the circulation of the WBC through the body (Lab Test Online, 2007).

2.1.3 Grading and staging of tumors

Steps to take in treatment planning are to determine the clinical extent of disease and specifically to determine whether the tumor is incurable by local treatment measures. The staging process requires radiological studies and biopsies of suspicious lesions and plays an important role in planning therapy (Chabner & Longo, 2010). The grading and staging of the tumors are the means of evaluating the tumor for malignancy or not.

- *Grading* of a tumor is according to their microscopic appearance, which indicates the degree of undifferentiation (anaplasia) present in the cells. The less differentiation of the cells, the more malignant the cancer.
- The importance of *staging* is in order to determine the anatomic extent of the cancer before therapy can be prescribed for the patient.

Staging is used to analyze and compare groups of patients. When this analysis are done the agreement on the following aspects is taken: 1) selection of primary and adjuvant therapies, 2) estimation of prognosis, 3) assistance in evaluation of the results of treatment, 4) facilitation of the exchange of information among treatment centers, and 5) contribution to the continuing investigation of human cancers (Greene, 2002).

The TNM staging were set up to determine the above diagnoses of a cancer patient:

- T - tumor size (T)
- N - the spread of the cancer to regional lymph nodes (N),
- M - the presence or absence of distant metastasis (M).

According to Table 2.1 below, the TNM staging will show how the size, spreading and presence or absence of distant metastasis may predict the stage of the cancer.

Table 2.1: The Basic TNM system identified four stages (Schneider *et al.*, 2003).

| Tumor stage | Tumor size | In the Lymph nodes | Metastasis |
|-------------|-----------------|-------------------------|------------|
| I | <2 cm | None | None |
| II | 2-5 cm | No, or yes on same side | None |
| III | >5cm | Yes on same side | None |
| IV | Does not matter | Does not matter | Yes |

The TNM staging system is used for data collection and coding for national or international cancer registrars, it is critical that the system is reproducible for institution to institution (Singletary *et al.*, 2002).

2.2 CANCER TREATMENT AND THE PHYSIOLOGICAL SYSTEMS

Patients with cancer undergoing treatment present unique issues to the health care team (Young-McCaughan & Arzola, 2007). Due to the fact that cancer could be a chronic and very complex disease, it is suggested that health care professionals with varied background are needed for comprehensive care (Gerber, 2001). All the different treatments coming from a multidisciplinary team will have an influence on the cancer patient. These different interventions are to the benefit of the patient in most cases, but it does have an impact on physiological- and psychosocial systems. According to Adamsen *et al.* (2009) being diagnosed with cancer and exposed to cancer therapies like chemotherapy, disrupts the patient's life, affecting physiological and psychological functioning and contributing to negative effects on the global health status/quality of life.

In most cases when an individual undergoes treatment for a cancerous tumor or illness, the treatment of chemotherapy causes the patient to become very ill due to these chemicals in their bodies. The treatment of chemotherapy and the other adjuvant therapies like radiation therapy, hormonal therapy and immunotherapy are in most cases beneficial for the patient, but the patient pays a high price due to the outcome of the side-effects that they experience during and after the treatment. Side-effect of

anticancer chemotherapy can be so difficult to live with that some patients regard it as worse than the illness itself (Lerman *et al.*, 1990).

All of these treatments cause physiological alterations to normal tissue and body function. Severe side effects include toxicities in many body systems and organs. Toxicities depend on choice of therapy, dose and the patient's tolerance. These toxicities have a huge impact on any cancer patient's quality of life (Schneider *et al.*, 2003).

General damage caused to physiological systems by

1. Radiation therapy can cause acute and chronic effects.
 - Acutely, reproducing and repairing cells are affected;
 - Chronically, necrosis, fibrosis, fistula formation, ulcerations and damage to specific organs occur (DeVita *et al.*, 2008).
2. Chemotherapy can damage bone marrow and leads to anemia or a loss in red blood cell count. The deficit of red blood cell leads to a decrease in oxygen transport to different tissue or cells. The deficit of RBC is called anemia. Oxygen deficit could develop in the cells and tissue, due to a low RBC count, may lead to necrosis or muscle wasting (Wilkes & Ades, 2004).

The cancer patient can experience cardiovascular-, pulmonary-, gastrointestinal-, musculoskeletal-, neuroendocrine-, nephro- and dermatological toxicity (Schneider *et al.*, 2003).

One of the main side-effect that I want to focus on in this study is *fatigue* that a patient experience during his or her cancer treatment. Anemia could be one thing that may cause fatigue, according to the FACT-F (fatigue), FACT-An (Anemia) and FACT-G (Cancer therapy) scales which have questions that tests the relevancy of fatigue in the treatment of cancer (Cella, 1998).

According to Gerber (2001), cancer patients that are being treated today live longer. The management of these patients is getting better and for example the challenge to become more active, not only in everyday tasks, but in terms of exercising. This means that health professionals are creating higher expectations of the patients' involvement and participation in his or her treatment program.

During the treatment period, there are different phases that the patient will go through and certain symptoms and needs the patient will learn to know in a specific phase they are in. In Table 2.2 below, it will give an overview of these rehabilitation-related issues.

Table 2.2 : Rehabilitation-related issues for Cancer Patients (Gerber, 2001).

| <u><i>Phase of cancer</i></u> | <u><i>Patient needs</i></u> | <u><i>Symptoms</i></u> | <u><i>Impact of symptoms on function</i></u> |
|---------------------------------|--|---|---|
| I. Pre-treatment and evaluation | Information about treatment options and impact of illness | Pain Anxiety Depression | Daily routines Sleep/fatigue |
| II. Treatment | Information Support Rehabilitation interventions Help with daily routines Vocational, home, etc. | Pain Anxiety Loss of mobility Wound/skin care Speech/swallowing | Daily routines Sleep/stamina Self-care Cosmesis Communication |
| III. Post treatment | Support Rehabilitation intervention | Pain/weakness Anxiety/depression Loss of mobility Edema Fatigue/stamina | Sleep/fatigue ADL Vocational/avocational Cosmesis |
| IV. Recurrence | Education | Pain/weakness | Sleep/fatigue |

| | | | |
|----------------|---|--|--|
| | Support Rehabilitation intervention | Anxiety/depression Fatigue/stamina Edema Bony instability Anorexia | Disability Disruption of routines Cosmesis Vocational/avocational |
| V. End of life | Education Support Palliative rehabilitation | Pain Fatigue Anorexia | Dependence Immobility |

Treating the cancer patient as a Biokineticist or Exercise specialist, must realize that the different treatments of the cancer patient, including exercise intervention, affects the patients quality of life. So the information to keep in mind is the patient's well-being at times during treatment and after treatment. This also means what type of intervention therapy and at what rate do they get these treatment or treatments. This will indicate the intensity of the adjuvant therapy of exercise intervention should be.

2.2.1 Fatigue

2.2.1.1 What is fatigue?

In the general population, fatigue is a non-specific symptom that may occur in conjunction with mental and other physical diseases. Fatigue may occur without the presence of any disease. In the general medical population, fatigue occur twice as much in women than in men (Stasi *et al.*, 2003). It is also said that the origin of fatigue in the cancer setting is certainly multifactorial; however, psychological factors seem to play an important role (Dimeo *et al.*, 1997).

Fatigue is one of the most frequent and distressing symptoms experienced by patients with any type of cancer. It is a self-recognized subjective phenomenon that accompanies both the disease and the treatments of cancer (McQuestion, 2009). Most patients with cancer experience fatigue, a severe activity-limiting symptom with

multifactorial origin (Lucia *et al.*, 2003). Most of these origins of fatigue will include radiotherapy or chemotherapy and therefore a common side effect of these cancer therapies.

A number of disease-related and treatment-related factors may contribute to fatigue. The impact of fatigue on QoL of the cancer patient is relevant (It may vary in frequency, intensity, onset, quality, pattern and meaning, and may be described in terms of sensations or by the ability of the patient to participate in activities. The fatigue experienced by patients with any type of cancer is not easily dispelled by sleep and interferes with activities and roles that give meaning and value to life (McQuestion, 2009).

Cancer related fatigue is far more disruptive to cancer patients' quality of life than in any other patients with almost any other disease. CRF has a very rapid onset if we compare it to the usually types of fatigue. It cause distress in the cancer patient and could impact on a lot of domains of the patient's ADL's, like social, physical, spiritual etc. The patient does not only experience it, they suffer with it (Holley, 2000).

The criteria that have to be met to make a diagnosis of CRF certainly are more specific than the simple question, "do you feel tired?" (Stasi *et al.*, 2003).

There are a few ways Cancer Related Fatigue (CRF) is described by patients and researchers.

- It is state of weariness after a period of exertion, mental of physical, characterized by a decrease of work capacity and reduce efficiency to respond to stimuli (Stasi *et al.*, 2003),
- Brown *et al.* (2006) describes it as a feeling that interferes with usual daily functioning,
- Psychobiological Entropy model by Winningham defines fatigue as an energy deficit that, if persistent, leads to a cycle of decreased activity, fatigue, and reduced function, which results in disability (Ream *et al.*, 2006).
- It may also be described or expressed as physical, affective, cognitive, attitudinal

and behavioral experiences (Winningham *et al.*, 1994).

- Then the National Comprehensive Cancer Network defines CRF as a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer-related treatment that is not proportional to recent activity and interferes with usual functioning (Velthuis *et al.*, 2009).

From the above-mentioned definitions of fatigue, we can see that it all comes down to how debilitating it is to the patients' well-being and mostly their quality of life (QoL).

2.2.1.2 Pharmacological and non-pharmacological treatment of CRF

Radiotherapy has been especially well recognized as a cause of fatigue, with up to 90% of patients experiencing fatigue during a course of radiotherapy (Brown *et al.*, 2006). Nonpharmacological interventions have been explored to treat fatigue in this population. One example was supportive-expressive group therapy that did seem to have an effect on fatigue and better the QoL of the patients. Although certain randomized controlled trials did show that this type of therapy was not that successful in most cases (Brown *et al.*, 2006). In contrast to the supportive-expressive group therapy done by Brown *et al.* (2006), physical exercise have improved fatigue for cancer patients in a number of randomized controlled trials. In prior studies, rest and non-exercise was prescribed, but this led to muscle catabolism or muscle wasting and this caused even more fatigue response in patients. Scientific evidence therefore gave the information that exercise of low to moderate intensity will battle CRF and improve the quality of life of these patients (Lucia *et al.*, 2003).

Then a study done by Velthuis *et al.* (2009) has also proven the fact that physical exercise shows promise in preventing and reducing complaints of CRF. The rationale supporting exercise intervention for CRF is based on the proposition that the combined effect of the disease, the medical intervention and a decreased level of activity during treatment cause a reduction in physical capacity.

2.2.1.3 Prevalence of fatigue

In Western societies, one in three people will experience cancer once in their lifetimes and one of their most frequently reported complaints with cancer is fatigue (Velthuis *et al.*, 2009). It is important to mention that the prevalence of CRF will not only affect the patient, but also their caregivers or family. In a study done by Stasi *et al.* (2003) they did a study of prevalence of CRF among cancer patients of randomly selected American families through interviews by telephone. These selected patients were diagnosed different types of malignancies which included breast cancer, leukemia's, lymphomas amongst others. They all received normal cancer treatment modalities like, chemotherapy, radiotherapy. In this study they found that 78% suffered from CRF.

A large proportion of patients had significant fatigue at baseline (before the initiation of radiotherapy), consistent with the reported literature concerning advanced cancer patients. Fatigue is present in 56 - 75% of cancer patients at the time of diagnosis, and the prevalence increases to over 90% for patients undergoing chemotherapy or receiving radiotherapy (Brown *et al.*, 2006). The prevalence of fatigue in 2002 according to the National Cancer Institute of the USA, showed a 72 - 95% of patients receiving cancer therapy that experience a debilitating fatigue resulting in diminished work capacity. In a later study done in 2006, it was prevalent in patients undergoing chemotherapy, and it was reported to affect 82 - 100% of all cancer patients (Ream *et al.*, 2006). Still in 2009, studies show that 60 - 96% of cancer patients reports cancer-related fatigue (Velthuis *et al.*, 2009). According to a study done by Dimeo in 2001, CRF may become long lasting problem and affect almost 30% of cancer survivors till long after the illness or end of treatment.

If we look at the above statistics, we will see that the prevalence has not changed in the last decade and intervention to improve fatigue are urgently needed.

2.2.1.4 Cancer treatment and fatigue

Cancer is usually accompanied by an “asthenic syndrome” consisting of two components, one objective (loss of physical performance) and one subjective (fatigue) (Dimeo *et al.*, 1997).

According to surveys, fatigue, due to cancer treatment is among the most frequent and burdensome side effect (Adamsen *et al.*, 2009). It is also stated that fatigue is one of the most severe imposers of normal daily activities and it may limit it tremendously (Dimeo *et al.*, 1997). Whereas most side effects are drug specific, fatigue is associated not only with most anti-neoplastic drugs but also with the disease itself (Adamsen *et al.*, 2009).

Fatigue patterns vary over the course of, and with the type of the therapy:

- Chemotherapy: Pickard-Holley found in 1991 that in most patients, fatigue occurred 3 – 4 days following chemotherapy, became more severe 10 days following chemotherapy and declined until the next cycle of chemotherapy (Schneider *et al.*, 2003). In a study by Young-McCaughan and Arzola (2007), showed that breast cancer patients that had been exercising during chemotherapy had a stable fatigue level according to their control group of no-exercising that showed a higher fatigue level.
- Surgery: It was found that postoperative fatigue was physiological in nature and did not have psychological determinants (Christensen & Hehlet, 1993). Fatigue in relation to surgery is not as severe as the other treatments. Most of the fatigue occurs immediately after an operation and steadily decrease with time and recovery (Shipp & Wiggins, 2006).
- Radiation therapy: Greenberg *et al.* (1992) found that fatigue reached a maximum in the fourth week (average of 17 treatments) in women with breast cancer. The researchers found that the patients’ fatigue was biological in nature and was independent of depressive symptoms.

Due to the different treatments, a number of known mechanisms have the potential to contribute to the fatigue levels of cancer patients; like vomiting, diarrhea, loss of

nutrients and electrolytes. Then are factors like neurotoxicity (slower motor function), cardio toxicity (more stress on the heart), pulmonary toxicity (lowering of lung capacity), hepatotoxicity and nephrotoxicity (affects the liver and kidney functioning) and then obvious destruction of red blood cells that helps with oxygen delivery. All these factors cause fatigue in the cancer patient (Schneider *et al.*, 2003).

In recent studies, physical exercise shows promise in preventing and reducing complaints of cancer-related fatigue (CRF). The rational supporting exercise interventions for CRF are based on the propositions that the combined effect of the disease, the medical interventions and a decrease level of activity during treatment cause a reduction in physical capacity (Velthuis *et al.*, 2009).

2.2.1.5 Different perceptions of fatigue

Fatigue is usually stated as a normal phenomenon due to the fact that if a person do exercises or work, they tend to get exhausted and the fatigue they experience will only protect the body from exaggerated or harmful efforts (Dimeo, 2001).

But in the case of an illness like cancer, fatigue is a symptom that is rarely assessed systematically or managed effectively in patients that are diagnosed with cancer (Conn-Levin, 2005). Patients that experience the challenge of fatigue during their cancer treatment usually do not believe that exercise being a way of relieving this extreme tiredness. Inactiveness actually increases levels of fatigue (Conn-Levin, 2005). The patients describe it as one of the most troublesome symptoms, not least as it compounds symptom distress and impacts greatly on quality of life (Ream *et al.*, 2006).

The Fatigue Coalition did a study in 1998 and it showed the following results in Table 2.3.

Table 2.3 : Effect of fatigue on cancer patient (Schneider *et al.*, 2003).

| % | Affect |
|----|---|
| 78 | ADL |
| 61 | Fatigue more than pain |
| 60 | Physical well being |
| 61 | Work capacity |
| 51 | Emotional status |
| 57 | Enjoyment of life |
| 44 | Intimacy with their loved one |
| 57 | Limit their social activity |
| 49 | Cannot finished tasks |
| 48 | Could not walk far due to fatigue |
| 12 | Wanted to die |
| 16 | Treating fatigue is as important that treating the cancer |

Some health professionals are reluctant to treat these patients and most cases if they do treat them; it is at this time still poorly managed. In contrast to patients, physicians only 26% felt that fatigue affected their patients more that pain did. This was in the same survey done by The Fatigue Coalition in 1998. The physicians also did not agree with the patients as to the cause of fatigue: 55% overall, believed that cancer causes fatigue, while patients (54%) and caregivers (61%) felt that the cancer treatments cause fatigue. This could be the reason that 75% of the cancer patients accept fatigue as one of the side effects of cancer and carry on and do not tell their physicians about how they are affected by fatigue. Only 35% of physicians said in this survey that they do treat fatigue as a symptom (Schneider *et al.*, 2003). This discrepancy between the patient and the - physician makes it clear that a protocol must be incorporated by a health care professional like a Biokineticist or an Exercise specialist as well as other professionals to help the patients and their caregivers to assist them in coping with this side effect.

2.2.1.6 Exercise vs. resting and fatigue

Adamsen *et al.* (2009) have done a study with the main purpose to assess the effect of a multimodal group exercise intervention as an adjunct to conventional care, on fatigue, physical capacity, general well-being, physical activity and quality of life in patients with cancer. The best way to manage fatigue is to understand how and when fatigue occurs and to plan the daily activities accordingly like exercises.

This exercise intervention would then indicate whether it could be the correct approach to manage CRF. Although it was proven that exercise is an intervention method for fatigue during cancer treatment (Windsor *et al.*, 2009). It is also the case that patients can not adhere to the intensity of exercises due to the CRF, and this could cause problems. This could lead to a resting period during the cancer treatment.

When resting is prescribed, it must be for a short interval due to the fact that atrophy of muscles occurs very rapidly and strengthening of muscles is important to function properly. As stated in articles of research, inactivity decreases muscle development and most of the time muscle atrophy (Ingram & Visovsky, 2007). This makes the patient even weaker and even more fatigued. Fatigue and a reduction in physical ability are common and often a severe problem in cancer patients regardless of disease stage and modality of treatment (Dimeo *et al.*, 1997).

The exercise that the cancer patient needs to do is not necessarily strenuous exercises. Some people prefer walking, yoga, swimming or Thai Chi. These are exercises that help and are relaxing, not strenuous and help the patient's fitness level. It appears that a regular exercise may have roles across the disease trajectory in reducing fatigue (Ream *et al.*, 2006). Another important fact is during exercise, repetitive motion causes muscle hypertrophy and increased muscle mass (Ingram & Visovsky, 2007). Therefore exercise may help people with physical limitations and can do some exercises to help them do their ADL's (Conn-Levin, 2005).

A pretest-posttest design study done on breast cancer patients has shown that the patients who exercise had an improvement in their physical functioning and very important, their cardiorespiratory fitness (Ingram & Visovsky, 2007). Women that received adjuvant radiotherapy and chemotherapy for breast cancer that were physically active reported less fatigue. Walking programs during cancer therapies like radiotherapy showed an improvement in these patients' fatigue levels. Home-based moderate-intensity walking program also showed a reduction in their fatigue levels (Brown *et al.*, 2006). With this information it only depends on the physical activity of the patient. It does not matter if it is light, moderate or intense levels of activity, as long as the patient is active.

Patients that are undergoing cancer treatment that are also receiving exercise intervention must be treated uniquely due to the fact that this disease is very unpredictable in many cases (Young-McCaughan & Arzola, 2007). Battaglini *et al.* (2006) pointed out that rehabilitation for cancer patients is non-linear, unpredictable and varied. Knowledge of the pathophysiology of cancer and cancer treatment coupled with expert guidance from an exercise physiologist can guide health care team recommending exercise for their patients undergoing treatment.

If we look at the statements that have been made in the paragraph of treatment and fatigue in the body (2.2.1.3) that affects the cancer patient's fatigue level, it is important to maintaining those mechanisms like the lung function and its capacity with exercise as an example or liver- and kidney functioning with a proper diet and enough water consumption. Due to the fact that the overall health aspect is applicable in the section of fatigue, this type of fatigue can be explained according to pain experience, electrolyte imbalance, fluid disturbances, anemia, impaired nutritional status and weight loss. The changes in the metabolic active molecules is noteworthy due to its interaction with the tumor and the host defense system, then the drugs used and their action on the nervous system, and sleep disturbances due to it (Dimeo, 2001).

When a patient experience fatigue, they tend to rest, nap or just being inactive. Fatigue usually sets in to protect the body from exaggeration or harmful effort (Dimeo *et al.*, 1997). This type of fatigue, associated with cancer, may not be bettered with sleep. This worsening of the whole body tiredness will lead to further complications other than the physical implications of this illness, the “*psychological and psychosocial impact*”. Psychosocial problems often follow the diagnosis of cancer and subsequent chemotherapy (Adamsen *et al.*, 2009) and psychological problems will progress from diagnosis through the cancer treatment. Psychological factors play an important etiologic role in the genesis of cancer fatigue. Psychological aspects do have and influence on fatigue and this is where rest and sleep comes in. Nerenz et al. found a strong relationship between tiredness and the emotional distress experienced during treatment (Dimeo, 2001).

According to Dimeo (2001), depression is considered to be a contributor to fatigue in cancer patients. Sleepiness is just one of the symptoms of depression. Although, getting adequate rest or sleep is essential of managing fatigue. Daytime naps can be helpful, but the patient must not let it interfere with their sleep pattern at nighttime, this can cause insomnia for some patients (Conn-Levin, 2005). According to Ream *et al.* (2006) too much sleep and rest that is not correctly managed by means of setting certain patterns, can lead to even higher fatigue levels. The psychological benefits of exercise include reductions in anxiety, tension, depression and these reductions contribute to the well-being of the active person, which means less tiredness and fatigued feeling and less mood swings. Thus the important part of managing the patient’s fatigue levels during and after cancer treatment, therefore management of one’s energy levels by means of energy conservation is to prioritize activities or delegate certain tasks (Conn-Levin, 2005).

Physical training or exercise has been introduced to improve physical capacity and QoL and to reduce fatigue (Adamsen *et al.*, 2009). Dimeo (2001) show that physical activity results in secondary benefits, and he stated that it could improve mood state, which in will therefore lessen the feeling of depression and anxiety. In other words, physical

activity benefits not only the physical aspects, but also the psychological aspects of the patient.

According to the findings of Brown *et al.* (2006) where the result suggested that physical activity may be beneficial in reducing the fatigue associated with radiation treatment. Keeping with these findings, a simple home-base exercise program to group psychotherapy in a randomized controlled trial, resulted in significant improvements in fatigue, compared to only to psychotherapy alone. Psychosocial activities like relaxation and massage, has also proven to relieve pain, nausea, fatigue and increase the patient's feel of self-control and therefore it is also recommended as a adjuvant therapy for cancer patients (Adamsen *et al.*, 2009).

Although in a study done by Brown *et al.* (2006) about the exercise intervention, was a very small intervention group that did show a better in the QoL in the patients as well. Through these findings they believe that a larger group of recruiting patients will show a better clinical significance.

Determining the best way to treat cancer-related fatigue and facilitate patients' self-management of it has been the objective of a growing number of published intervention studies (Ream *et al.*, 2006).

The main aspect of this study is to proof as it has been proven in studies the last few years, that exercise intervention can lessen some of the side effects of cancer treatment. Treating the cancer patient as a Biokineticist of Exercise specialist, must realize that this treatment of the cancer patient, affects the patients quality of life. So the information to keep in mind is the patient's well-being at times during treatment and after treatment. This also means what type of intervention therapy and at what rate do they get these treatment or treatments. This will indicate the intensity of the adjuvant therapy of exercise intervention should be.

In Table 2.4 below it is indicated the different influences on fatigue by Dimeo (2001).

Table 2.4: Factors implicated in the pathogenesis of fatigue

Physiologic

- Underlying neoplastic disease
- Abnormalities of energy metabolism
- Decreased availability of metabolic substrates
- Abnormal production of substances inhibiting metabolism or normal muscle function
- Neurophysiologic changes of skeletal muscles
- Chronic stress response
- Hormonal changes

Antineoplastic treatments

- Chemotherapy
- Radiotherapy
- Surgery
- Biologic response modifiers

Concomitant systemic disease

- Anemia
- Infections
- Lung disease
- Liver failure
- Renal failure
- Malnutrition
- Neuromuscular disorder
- Dehydration or electrolyte imbalances
- Thyroid disorders
 - Sleep disorders
 - Immobility and lack of exercise

- Chronic pain
- Use of centrally acting drugs

Psychosocial

- Anxiety disorders
- Depressive disorders – Associated with stress
 - Associated with different environmental factors

2.3 EXERCISE FUNDAMENTALS AND CANCER PATIENTS

In the area of sport medicine, exercise in cancer is one of the least-studied areas in the literature. With the current studies that have been reported in the past ten years, there is much enthusiasm that exercise programming may have as much of an impact on survivorship as any other therapy (Durak *et al.*, 2001).

Most diseases affect a patient's physical function. Historically, patients with a chronic diseases like cancer where advised to rest and to avoid physical activity. However, excessive rest and lack of physical activity may result in deconditioning and thus result in functional capacity and QoL (Oldervoll *et al.*, 2003).

Exercise has been shown to be an effective self-help intervention for fatigue during cancer therapy (Windsor *et al.*, 2009). Throughout the years, exercise has been boosted as one of the best interventions for the human body to keep and stay healthy. Health of the human body includes the following systems being healthy: cardiovascular-, pulmonary functions, prevention of obesity, minimizing impact of ageing (Schneider *et al.*, 2003). Also in a growing body of research by researchers like Young-McCaughan and Arzola (2007), the investigations surrounding exercise in patients with cancer, dramatic improvements in physiologic and psychological functioning have been documented in patients participating in aerobic exercise programs.

The concept of exercise of keeping the whole body healthy and keep it sustained over a long period of time, also applies to cancer patients these days, after a lot of research

that has been done over the world. Cancer patients may also be limited by cancer therapy. This means that chemotherapy in cancer treatment may become a barrier to exercise (Windsor *et al.*, 2009). Patients' overall health in the process of cancer treatment must be taken into account though. The aspect of "no exercise" is not the problem, it will be the intensity.

Side-effects from cancer treatment may extent way beyond the end of treatment, despite of improvement of QoL. Evidence to support the efficacy exercise intervention on cancer patients reducing symptoms and improving QoL, comes from over 80 exercise interventions studies involving cancer survivors (Hayes *et al.*, 2011).

According to Durak *et al.* (2001) hypothesis was exercise safe and efficacious for cancer patients independent of location and instructional methods. Therefore, ANY exercise has a positive influence on the cancer patient, no matter where, when and how. Courneya (2006) stated that exercise consistently demonstrates beneficial effects on wide variety of quality of life outcomes regardless of the specific intensity, duration, and method of exercise prescription, cancer sit, cancer treatment, or intervention timing (In Durak *et al.*, 2001). Therefore exercise intervention has been included in a lot of oncologists or doctors' treatment intervention as an adjuvant therapy the last few years.

In cancer studies and specifically to lessen side effects of treatment as well as finding ways to boost the quality of life of the cancer patient, studies like Schneider *et al.* (2003) investigated the fact that exercise intervention can reduce the side effects of cancer treatment. It is important that exercise intervention is individualized, because the doctors or the clinicians that is part of the multidisciplinary team have to ensure the best way of outcome of that specific patient's health. The patient usually has needs, limitations, and has certain capacity for exercise intervention, and therefore the program needs to be specifically written or be unique to each patient.

The contention therefore, is that exercise that is individualized according to the patient's needs; limitations and capacity do have a place in the community and setting, in and out of hospital (Durak *et al.*, 2001)

2.3.1 Physiological adaptations of cancer patient to exercise

Exercise physiology is the study of how structural and functional aspects of the human body are altered when exposed to acute and chronic bouts of exercise according to the book, "Exercise and Cancer Recovery" by Schneider *et al.* (2003). Exercise causes a difference in the person's physical, anatomical and muscular systems throughout time. This means that the person can be monitored through different stages of exercise and see what type of exercise cause what system to develop or become better. For example aerobic exercise will cause the cardiovascular- and pulmonary systems to develop over a certain time period.

Despite the improving of physical capacity of the human body by means of exercise, it also improves the psychological aspects as well. The patient needs to adapt to psychological changes during this time as well. Physical activity has been suggested to affect the severity of fatigue by increasing plasma and brain tryptophan levels, which combats the decreased synaptic levels of 5-hydroxytryptamine found in cancer-related fatigue (Windsor *et al.*, 2009).

It is wise to exercise before beginning cancer treatment, because it can build up strength, flexibility, energy stores, endurance, and balance to better the patient for the effects of treatment. Exercise can help to regain the baseline of exercise testing levels. Exercise can also improve metabolism, normalize appetite, and help the body to rid itself of the drug's byproducts, which encourages healing. Exercise can also be a tension reliever (Shipp *et al.*, 2006). While working with a certain patient, a baseline of physiological information before initiating exercise intervention program (Schneider *et al.*, 2003). The reason for the baseline statistics will be to establish if the patient shows improvement of his or her condition or not.

Over the last few years the exercise intervention program has been incorporated into cancer treatment due to the fact of the benefits that exercise have on the human body (Schneider *et al.*, 2003). Exercise demonstrated the effect that regular exercise has on various systems in the human body, as it has been explained later in this study and the subsequent changes in the fitness status of the individual.

The changes, that may include fatigue and other deteriorating factors of what treatment may cause, in the cancer patient's fitness level can influence the quality of life. Exercise intervention could influence the cancer patient's QoL for the better, which implicate a positive influence as adjuvant therapy for cancer treatment. It is important to remember though, that the patient will go in for treatment and this could include hospitalization and it will lead to physical well-being deterioration. This inactivity could be devastating. Therefore, early intervention is the key to preventing problems that may occur due to the general weakness. It is easier to maintain strength, range of motion, and endurance rather than to regain it (Shipp *et al.*, 2006).

In a study by researchers where they studied different types of exercise interventions from aerobic, resistance and combination types, they found that no adverse events occurred and the adherence to exercise intervention programmes was moderate to excellent. It may then be concluding to this literature that a physical exercise program, supervised as well as home-based, during adjuvant cancer treatment is feasible and does not cause any additional health risks for cancer patients (Velthuis *et al.*, 2009)

Why me? That is a natural question, but I doubt if you'll ever get an answer. Why not me? The answer is because no one is immune. It is me! This is where you are today. Take it one day at a time, face what you're up against, assemble your plan to combat it, and most of all, and believe in yourself and your plan.

- Linda Kendall (Brain tumor survivor, diagnosed 1986)
(Armstrong *et al.*, 2004)

2.4 WHAT IS A BRAIN TUMOR?

A brain tumor is a mass of cells that have grown and multiplied uncontrollably. Brain tumors are divided into two categories namely primary brain tumors and metastatic brain tumors (Freedman, 2009).

- *Primary brain tumors* originate in the brain and very rarely spread to other parts of the body.
- *Metastatic brain tumors* or in other words, secondary tumors, come from cancer cells in another part of the body. The diseased cells spread to the brain by moving through the bloodstream. This is called *metastasis* (Armstrong *et al.*, 2004).

People diagnosed with a brain tumor are a significant small number compared to other cancers, but are included in cancer studies due to the heavy toll it exact on people affected by it (Panno, 2005).

Primary and metastatic tumors are a significant cause of morbidity and mortality in cancer patients worldwide (Molassiotis *et al.*, 2010). Argument in previous years by researchers a tumor in the Brain was not classified as cancer (Roberts & Musella, 2005). In this case the definition of cancer was given as a malignant tumor that can lead to potential death (Brown *et al.*, 2006). That is exactly what a tumor in the brain mend. Brain tumors are life threatening, and therefore it was classified as a cancer (Roberts,

2005). Brain tumors can be cancerous or noncancerous. Both types take up space in the brain and may cause serious damage to the brain or cause symptoms like vision- or hearing loss or other complications. Cancerous tumors or malignant tumors are life-threatening due to their invasive and aggressive behavior. Noncancerous tumors or benign tumors are also life-threatening if it should compromise any vital structures (Yang, 2006).

2.4.1 Classification of brain tumors

The World Health Organization (WHO) classifies primary brain tumors based on cellular origin and histologic appearance (Chandana *et al.*, 2008). The St. Anne/Mayo grading system is based on four features namely nuclear atypia, mitotic figures, microvascular proliferation, and necrosis. Starting with a baseline score of 1, all features are given 1 point, and an additive score is made (Glioblastoma Multiforme Grade IV is the maximum grade) (Mischel & Vinters, *In*: Liao, 2001). For easier understanding of brain tumors they are named for the cell type of origin and some are name according to their location. Most medical institutions are using the WHO classification system to identify brain tumors. This classification system can be seen in Table 1.1 on page 17 in the Introduction (Armstrong *et al.*, 2004). In some cases, doctors will diagnose a *cerebral tumor* to classify a tumor originates in the skull indefinite to where it is situated at that moment (Brown *et al.*, 2006).

The classification helps with the grading of the tumor in order for the doctors or oncologists to help predict its likely behavior and with treatment (Armstrong *et al.*, 2004). This means that the tumor will either be classified as benign or malignant.

In this study, the focus is on primary brain tumors. As previously said in this section this type of tumor originates in the brain itself and rarely spread to other parts of the body (Armstrong *et al.*, 2004).

2.4.1.1 Primary brain tumors and possible causes

The question that has been asked many times is who gets brain tumors and why?

Does the development of a brain tumor run in a family? Several central nervous system (CNS) tumors are associated with rare genetic conditions. The most commonly is autosomal dominant disorder neurofibromatosis 1 (Chandana *et al.*, 2008). Armstrong *et al.* (2004) support this theory where they believe that the only proven causes of brain tumors are rare hereditary syndromes (*tuberous sclerosis, Von Hippel Lindau syndrome and neurofibromatosis types 1 and 2*), therapeutic radiation, and immunosuppression that give rise in brain lymphomas (Armstrong *et al.*, 2004). Some people have a rare gene or chromosomal abnormality that greatly increases their chance of developing brain tumors. Genetic predisposition, as it is called, probably accounts for less than five percent of brain tumors (Wrench, 2008).

Questions then arose about possibility that diet, pesticides, chemical exposures and certain industries where worker are expose to carcinogenic or toxic substances may cause brain tumors. Some neurologists have suggested a possible connection between head injury and meningioma, but most experts disagreed (Ma, 2006). In diet, studies have been done that a substance known as N-nitroso compounds have been clearly identified as carcinogenic to the nervous system. N-nitroso compounds are present in cured meat (nitrites), cigarette smoke, cosmetics and many other sources. These compounds are also produced in the human body as the digestive process breaks down food (including vegetables) and drugs. Some studies of diet and vitamin supplementation seem to indicate that dietary N-nitroso compounds might influence the risk of both childhood and adult brain tumors (Armstrong *et al.*, 2004). According to Chandana *et al.* (2008) in the studies done by Armstrong *et al.* (2004), the evidence remain inconclusive.

Compelling evidence from workers that are in the production of synthetic rubber and polyvinyl chloride and workers in certain parts of the petrochemical and oil industries are at greater risk for developing brain tumors. There are however, these studies are also contradictory and inconclusive like the above paragraph's questions according to Armstrong *et al.* (2004).

Does exposure to electromagnetic fields cause brain tumors? This is probably the most asked question as well as cellular radiation (cell phones) and radio frequency (RF) that could be causes of brain tumor development. According to Wrench (2008) a number of studies have shown a significantly increased risk of 10 - 20 % for brain cancer among electrical workers. Although it cannot be said that workers exposed to higher levels of electromagnetic field is more in danger than those exposed to lower levels. There are still limitations in this area and there is no evidence that power frequency electromagnetic field can cause cellular mutations, and the evidence such exposures might promote tumors is hotly debated (Wrench, 2008). A new study (Deltour *et al.*, 2009) done over a period of 30 years in Scandinavia, found no substantial change in prevalence even after cell phone use became widespread, according to the report in the December 2 online edition of the Journal of the National Cancer Institute in 2009, therefore it supports the study done by Bondy *et al.* (2008). Despite of this study, this question will not go away. Scientists believe that the growing in cell phone usage these days have not shown a notable increase in brain tumors. This can also mean that, according to Deltour and colleagues, that cell phones don't cause brain tumors or it means that we don't see it yet or we don't see it because the increase is too small in the population that they have studied so far or that it is limited to a small subgroup of the population (Deltour *et al.*, 2009).

It is important not to confuse radio RF with ionizing radiation, such as x-rays or gamma rays. RF fields cannot cause ionization or radioactivity in the body; therefore RF fields are called non-ionizing. The relationship between cell phone usage and development of brain tumors are inconclusive and there is no association. Although, this study was conducted a few years back and cell phone use were not that common (Armstrong *et al.*, 2004). Not one study of the above done on brain tumor diagnosis could prove any of these probable causes (Bondy *et al.*, 2008). Advances in genetic research may shed light on what makes a person susceptible or resistant to developing a brain tumor (Armstrong *et al.*, 2004). In Table 2.5 below, the summary of possible risk factors of Primary Brain Tumors are listed:

Table 2.5: Risk factors for Primary Brain Tumors (Chandana *et al.*, 2008).

| <u>Environmental</u> | <u>Genetic</u> |
|--|---|
| <p data-bbox="181 450 292 483"><u>Proven</u></p> <ul data-bbox="231 501 596 535" style="list-style-type: none"> • High-dose of ionization <p data-bbox="181 611 331 645"><u>Unproven</u></p> <ul data-bbox="231 663 778 1462" style="list-style-type: none"> • Alcohol use • Cellular telephones • Chemical agents (e.g. hair dyes, solvents, pesticides, traffic-related air pollution) • Extremely low-frequency electromagnetic fields • Head trauma or injury • Infections (e.g., viruses, toxoplasma gondii in utero influenza, varicella) • Nitrosamine, nitrosamide, nitrite, nitrate or aspartame consumption • Occupational exposures (e.g., rubber viny chloride, petroleum) • Tobacco use | <ul data-bbox="858 450 1394 925" style="list-style-type: none"> • Li-Fraumeni syndrome (P53 mutation) • Multiple endocrine neoplasia type 1 • Neurofibromatosis 1 and 2 • Nevoid basal cell carcinoma syndrome • Tuberous sclerosis • Turcot's syndrome • Von Hippel-Lindau syndrome |

2.4.2 How to understand the brain

When diagnosed with a brain tumor, the first step is to understand the brain. Different types of tumors that develop in areas that are influenced in the brain, cause different signs and symptoms to the patient.

The brain is a soft, spongy mass of nerve cells and is connected to the spinal cord. There are 4 ventricles or hollow spaces in the middle of the brain and contains the *choroid plexus* structure that produces cerebrospinal fluid that circulates throughout the

central nervous system (CNS) (Armstrong *et al.*, 2004; Brown, 2006). The skull, spinal column and meninges protect the brain and spinal cord from external influences or damage.

The following will be a short overview of different parts in the brain where tumors can occur and their main functions:

2.4.2.1 Spinal cord

The part of the central nervous system that extends from the brain to run within the spinal column as far as the second lumbar vertebra, where it continued by the *filum terminale*, a fibrous cord extending to the second piece of the sacrum, where it is anchored (Brown, 2006).

The CNS consists of nerve fibers and supportive cells and relay messages to the rest of our body. The peripheral nerves system (PNS) is made up of nerves that connect the CNS to the sensory organs, muscles, blood vessels and glands.

2.4.2.2 Cerebrum

This is the largest area in the brain and consists of a left and a right hemisphere. The right hemisphere controls the left side of the body, whereby the left hemisphere the right side of the body control.

- *Cortex*: the outer layer of the cerebrum that is made up of nerve cells called the *gray matter*.
- *White matter*: the internal layer of the cerebrum that is made up of nerve cells called the *axons* (Armstrong *et al.*, 2004; Brown *et al.*, 2006)

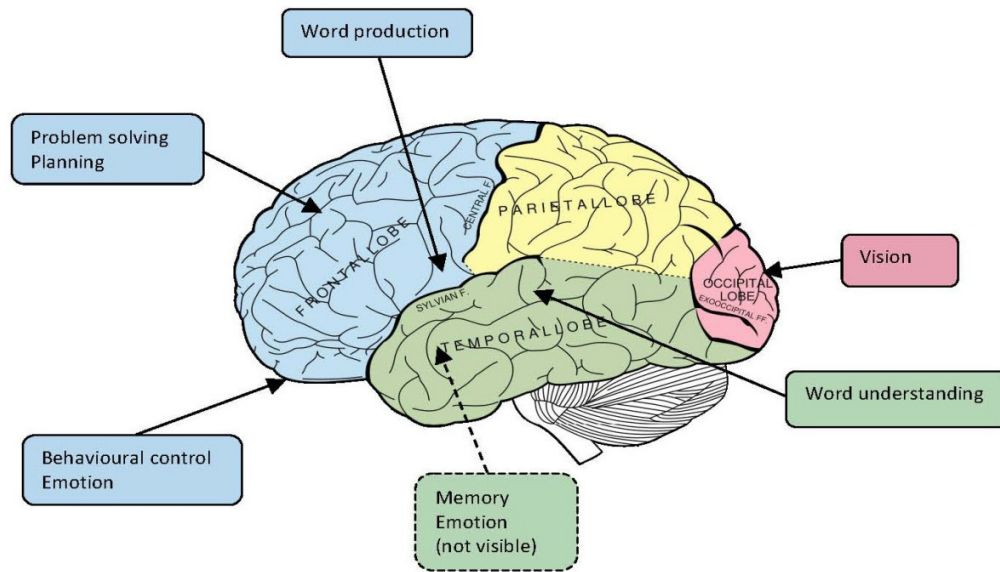


Figure 2.1 : Different brain lobes and functions
 (http://en.wikipedia.org/wiki/Human_brain).

The cerebrum consists out of four different lobes with different functions:

1. **FRONTAL LOBES:** These lobes make up the front portion of the cerebrum. It deals in the function of *attention, abstract thought, problem solving, intelligence, creative thought, initiative, inhibition judgment, moods, major body movements, bowel and bladder control, memory and reasoning* (Armstrong *et al.*, 2004).
2. **PARIENTAL LOBES:** Situated in the upper central portion of the cerebral hemispheres. These lobes *process all messages being sent to and from the brain regarding physical sensation* for example shape, spatial orientation, weight, texture and consistency (Armstrong *et al.*, 2004).
3. **TEMPORAL LOBES:** These lobes form the lower portion of the cerebral hemispheres. These lobes manage most auditory activities in the brain by translating words into meaning (Brown *et al.*, 2006). There is also a very small important portion of these lobes that controls intellect and the brain's ability to preserve long-term memory patterns. The left temporal lobe is also more dominant due to the controlling of speech in most speech (Armstrong *et al.*, 2004).

4. OCCIPITAL LOBES: These lobes are situated in the back portion of the cerebral hemisphere. The occipital lobes control vision and reading (Brown *et al.*, 2006). The right occipital lobe processes what is seen in the left field of vision and the left occipital lobe processes what is seen in the right field of vision (Armstrong *et al.*, 2004).

2.4.2.3 Thalamus

It is situated in the center of the two hemispheres above the hypothalamus. The thalamus acts as a pathway for most messages that pass to and from the brain and is responsible for our conscious awareness of pain, focusing of attention, certain aspects of speech/language and the sleep/wake cycle (Armstrong *et al.*, 2004).

2.4.2.4 Hypothalamus

This is the part of the brain that lies at the base, below the third ventricle and below the thalamus. Its integrity is essential for life, because it controls the “vegetative” function of the body namely; body temperature, appetite, blood pressure and fluid balance and sleep; it can also said to be the physical basis of emotion (Brown, 2006)

2.4.2.5 Pituitary gland

This gland is also called the *hypophysis*, and is found at the part of the brain between and behind the eyes. This gland is connected to the hypothalamus. The hypothalamus transmits messages to the pituitary gland telling it to secrete the hormones that regulate growth, blood pressure, the thyroid and gender-related functions (Armstrong *et al.*, 2004). The pituitary gland also produces a hormone that controls the rate of water that is secreted into the urine. This controls the amount of water in the body. Part from this function, this gland secretes the eight most important hormones in the body, that will not be discussed in this study (Brown *et al.*, 2006).

2.4.2.6 Brain stem

The brain stem is located at the base of the skull, includes the *medulla, pons and midbrain* (Armstrong *et al.*, 2004). From the brain stem emerge twelve cranial nerves

that control hearing, vision, sense of smell and balance (Brown *et al.*, 2006) and from the spinal cord 31 pairs of mixed sensory and motor nerves which runs to all parts of the body. It controls involuntary functions, including breathing. All functions controlled by the cerebrum pass through the brain stem (Armstrong *et al.*, 2004).

2.4.2.7 Cerebellum

The cerebellum is the part of the brain which occupies the posterior fossa of the skull behind the brain stem (Brown *et al.*, 2006) and has many connections to the brain and the spinal cord. The cerebellum is responsible for coordinating muscle groups and controlling small movements and balance (Armstrong *et al.*, 2004).

2.5 THE DIAGNOSING AND SYMPTOMS OF A BRAIN TUMOR

The symptoms from primary brain tumors can be physical (e.g. fatigue, headaches), emotional (e.g. depression and anxiety) and neuro-cognitive (e.g. decrease in attention and concentration, memory loss) (Shaw & Robbins, 2006 In: Molassiotis *et al.*, 2010).

According to Armstrong *et al.* (2004) a brain tumor is usually suspected if symptoms of severe headaches, faint spells or seizures and focal deficit are experienced. Although through my experience in literature studies and personal experience, some of these patients do not always express all of these symptoms. A brain tumor, in most cases, causes a block to cerebrospinal fluid's flow between the ventricles in the brain, causing a build-up of fluid and the swelling. This is called *brain edema* and this may lead to extensive complications. While there is information regarding symptoms of brain tumors, little is known how the symptoms affect or the type of impact it has on the patient's everyday life (Molassiotis *et al.*, 2010)

2.5.1 Symptoms of a brain tumor

The most common symptoms of a brain tumor are:

- Headaches, that are most severe in the morning (Armstrong *et al.*, 2004; Molassiotis *et al.*, 2010);
- Seizures or convulsions;
- Speech and language difficulties (Molassiotis *et al.*, 2010);

- Personality changes (Armstrong *et al.*, 2004)
- Tumor affects walking, movement and balance (Armstrong *et al.*, 2004);
- Deafness (Ma, 2006);
- Ringing in ears; and
- Dizziness and vertigo (Ma, 2006).

According to Table 2.6 below, the area of the tumor will indicate the form of symptom that the patient will experience:

Table 2.6 : Focal neurologic signs and symptoms of Primary Brain Tumors (Chandana *et al.*, 2008).

| Tumor location | Sign and symptoms |
|----------------|---|
| Frontal lobe | Dementia, personality change, gait disturbance, expressive aphasia, seizure |
| Parietal lobe | Receptive aphasia, sensory loss, hemianopia, spatial disorientation |
| Temporal lobe | Complex partial or generalized seizure; behavior change, including symptoms of autism, memory loss and quadrantanopia |
| Occipital lobe | Contralateral hemianopia |
| Thalamus | Contralateral sensory loss, behavior change, language disorder |
| Cerebellum | Ataxia, dysmetria, nystagmus |
| Brain stem | Cranial nerve dysfunction, ataxia, papillary abnormalities, nystagmus, hemiparesis, autonomic dysfunction |

A study done by Armstrong *et al.* (2004) on 124 brain tumor patients, it was shown that the most common symptoms experienced were constitutional in nature, including fatigue, sleep disturbances, drowsiness, distress and dry mouth. Six symptoms that

mostly influence the quality of life of the patients are fatigue, uncertainty of the future, motor difficulties, drowsiness, communication difficulties and headaches were reported in more than 50% of patients with a glioma in this study (Molassiotis *et al.*, 2010).

There are many more symptoms that can be connected to the diagnoses of a brain tumor, but this depends on the location of the tumor and what type of system it affects for example, a tumor to the anterior pituitary gland, will cause an hormonal imbalance or pressure on the optic nerve (Ma, 2006).

According to Van der Ham *et al.* (2010), they had two cases of patients having trouble with certain aspects of normal daily activity, like acknowledging places or finding places. The two cases studies brought them to these scientists attention that after self-reported difficulties by the patients, they have experienced problems with navigation. It is therefore important to test it by examining the separate elements to find out where those impairments in the brain lie exactly.

2.5.2 Diagnosing of a brain tumor

If a person suspects that he or she has symptoms that may relate to a brain dysfunction, their house doctor will refer them to a specialist for evaluation. A battery of tests will be performed by a *neurologist* to detect the symptoms of the patient and identify where the tumor area. These tests will make it easier to locate the tumor. This is called a *neurological examination* (Armstrong *et al.*, 2004).

Most brain tumors are diagnosed by means of a biopsy. Although, a battery of test will first be done by a doctor or an *oncologist* to detect what type of symptoms the patient experience and identify where the tumor could originate and make locating the tumor easier. This is called a *neurological examination*.

A neurological examination includes physical and neurological alertness tests as well as medical history like questions the following:

- How the patient feels at present;

- When the patient first noticed the symptoms;
- Are the symptoms worsening;
- Intensity and location of the headaches; and
- Changes in vision and other sensory organs (Armstrong *et al.*, 2004).

After the neurological examination, a scan will then be performed and will then show the internal structure of the brain from various angles. Some types of scans use a contrast agent where the abnormal tissue in the brain absorbs most of the dye and that show the doctors the difference between the healthy tissue and the abnormal tissue, in this case, the tumor (Armstrong *et al.*, 2004). The most common scan used is the MRI scan, this is a three dimensional image, to detect the precise area of the tumor by means of largeness and area affects (Armstrong *et al.*, 2004). The functional magnetic resonance imaging (fMRI) is a noninvasive technique for analysis of brain function that uses changes in blood oxygenation to identify areas of increased and decreased neuronal activity. The technique has in fact proven to be extremely valuable, allowing researchers to localize the representation of sensory, motor, and cognitive processes. Although this preoperative fMRI has its limitations due to the patient's ability to perform the tasks that the neurosurgeon wants them to perform to localize the area that has been affected by the tumor (Zhang *et al.*, 2009). When the scan or MRI is done, a biopsy is usually scheduled to determine the type of cell and tumor type the patient will be diagnosed with.

2.5.3 Analysis of brain tumor tissue

A *neurosurgeon* removes tissue from the tumor and sends it for analysis by a *neuropathologist* (Henson, 2005). When neuropathologists analyze tumor tissue under a microscope main questions being asked:

1. What type of brain cell did the tumor arise from? The answer usually gives the tumor a name for example Astrocytoma ; and
2. Do the tumor cells show signs of rapid growth? This assigns a tumor with a grade, such as grade III or IV.

The pathologist's report contains the analysis of the brain tissue. The answers from the above mentioned questions arose here. The tissue gained from the craniotomy or the needle biopsy, contains the diagnosis of the tumor type. Sometimes the neurophysiologist cannot make an exact diagnosis due to different type of cells (different grade types) in the tissue that was resected. This could lead to a miss diagnosis; this is called a *sample error*. Like for instance, the recognition of oligodendroglial component in anaplastic tumors and tumors with mixed cells subpopulations is highly important, not only from a mechanistic point of view but also with regard to rational therapeutic approaches (Martinez *et al.*, 2005). Due to this possible mistake or error, this sample may be send to a different institution for diagnosis (Armstrong *et al.*, 2004). The percentages of cells that are actively dividing within the tumor are measured by a test called the *MIB-1 labeling index*. If no cells are actively dividing the MIB-1 labeling index (LI) would be expected to be 0%. An MIB-1 labeling index of greater than 30% indicates that the cells are growing rapidly (Armstrong *et al.*, 2004).

The two answers that are gained from neurophysiologist's analysis after a biopsy or resection are then combined and the treatment options, prognosis and other necessary information are given to the brain tumor patient and their families (Henson, 2005). The diagnosing of the physical aspects of primary brain tumor in the patient's is not the only aspect that must be taken into consideration when preparing for treatment. A multifaceted approach has the potential to better define the relative risks versus benefits of different treatment protocol, particularly when they exhibit small differences in terms of survival benefit (Armstrong *et al.*, 2004). This has to include the process of adaptation by the patient and his or her family's to the emotional and psychological impact of this illness.

2.5.4 Tumors origination

Tumors originate out of different types of cells and can be made up of different kinds of cells for example the malignant tumor called Glioblastoma Multiforme. Severe and aggressive tumors that originate in specialized cells are cells that form the protective sheaths of nerve fibers (Ma, 2006). Tumors can arise from the meninges, the fibrous

tissues that cover the brain's surface and spinal cord, and they account for 19% of all primary brain tumors. It can also develop from the meningeal layer anywhere, but common locations are on the surface of the brain and near the bone structure at its base (Ma, 2006). Glioblastoma Multiforme (GBM) is the most common lethal primary central nervous system tumor in adults. GBM is rare in childhood and adolescence as primary intraventricular tumors (Sarsilmaz *et al.*, 2010), but there are reports that significant differences exist in the location of GBM according to age groups (Sarsilmaz *et al.*, 2010). A study by Jahraus *et al.* (2003) reported an atypical GBM located in the brain stem in a 6-year-old girl, and De Prada *et al.* (2006) reported a giant cell Glioblastoma in an 11-year-old girl, which is very rare (In: Sarsilmaz *et al.*, 2010).

2.5.5 Location of the brain tumor and adjustments by patient

There are many more symptoms that can be connected to the diagnoses of a brain tumor, but this depends on the location of the tumor and what type of system it affects for example, a tumor to the anterior pituitary gland will cause a hormonal imbalance or pressure on the optic nerve (Ma, 2006).

The patient that is diagnosed with a brain tumor will need to know what part of the human body will be affected in the process. The affected areas need to be considered in preparing and assisting the patients' adjustment to a difficult illness with poor prognosis, and attempt to improve impaired areas to life that are important for patients (Molassiotis *et al.*, 2010). According to the area of diagnosis and how the patients adjust, we can only guess how it affects each individual's daily lives (Molassiotis *et al.*, 2010). The different symptoms that patients might experience during their illness and what aspect or aspects of the daily lives will be affected; will usually indicate where the tumor is situated in the brain. According to Van der Ham *et al.* (2010), they had two cases of patients having trouble with certain aspects of normal daily activity, like acknowledging places or finding places. The two cases studied brought them to these scientists attention that after self-reported difficulties by the patients, they have experienced problems with navigation. It is therefore important to test it by examining the separate elements to find out where those impairments in the brain lie exactly (Van

der Ham *et al.*, 2010). The data that is available on the brain tumor population is mainly descriptive in nature (frequencies and intensity of symptoms) and does not highlight the meaning behind them from the patient's perspective (Molassiotis *et al.*, 2010).

The findings of the study done by Molassiotis *et al.* (2010) have shown the difficulty that the patients experience to verbally communicate their perception of their symptoms. Long-term survivors of brain tumors, which are a very small group but increase group of patients, seem to have a different outlook in life (Molassiotis *et al.*, 2010). As the concept of quality of life, as opposed to extending life, is central in this poor prognosis group, a coordinated effort from health care professionals, should take place early in the illness trajectory with involvement of a multidisciplinary team (Molassiotis *et al.*, 2010).

2.5.6 Pre-treatment assessment of patient

Pre-treatment of a brain tumor patient sometimes includes the Karnofsky scale (KPS) used to assess the patient's performance status (Karnofsky & Burchenal 1949 In: Meyers & Hess, 2003). The KPS does not address domains considered essential for measuring QoL, nor does it address cognitive impairment of a patient after they have been diagnosed with a brain tumor (Wade, 1992; Aitken, 1994 In: Meyers & Hess, 2003). The patient is usually still competent in ADL if his or her KPS-score is > 60 (Table 2.7). Some groups have improved on the KPS by using assessments that combine survival with the length of time patients have adverse effects of disease and treatment (Murray *et al.*, 1995 In: Meyers & Hess, 2003). Other groups are instituting more comprehensive and objective assessments of the patient's ability to perform activities of daily life (ADL) to supplement the KPS score (Brazil *et al.*, 1997 In: Meyers & Hess, 2003).

Table 2.7 : The Karnofsky Performance Scale (Crooks *et al.*, 1991).

| | | |
|---|-----|---|
| Able to carry on normal activity and to work; no special care needed. | 100 | Normal no complaints; no evidence of disease. |
| | 90 | Able to carry on normal activity; minor signs or symptoms of disease. |
| | 80 | Normal activity with effort; some signs or symptoms of disease. |
| Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed. | 70 | Cares for self; unable to carry on normal activity or to do active work. |
| | 60 | Requires occasional assistance, but is able to care for most of his personal needs. |
| | 50 | Requires considerable assistance and frequent medical care. |
| Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly. | 40 | Disabled; requires special care and assistance. |
| | 30 | Severely disabled; hospital admission is indicated although death not imminent. |
| | 20 | Very sick; hospital admission necessary; active supportive treatment necessary. |
| | 10 | Moribund; fatal processes progressing rapidly. |
| | 0 | Dead |

In Table 2.7 above, it shows different affects and experience of symptoms of brain tumor patients. By using this table, it will indicate how dependant or independent a patient is at a specific stage of the diagnosis. Sometimes this reading becomes worse and other times it may become better. In brain tumor patients' case, it gets worse in most of the time.

2.6 DIFFERENT TYPES OF PRIMARY BRAIN TUMORS

A booklet for Brain tumor patients and their caregivers has been researched and printed with the assistance of the National Brain Tumor Foundation in the US by Armstrong and colleagues. They have set up a range of what type of different brain tumors that can occur in the human brain.

According to studies done by Chandana *et al.* (2008), they found that neuroglial tumors account for more than 80% of primary brain tumors. These tumors derive from astrocytes, oligodendrocytes, or ependymal cells. Gliomas are divided into four grades (states by the WHO); grade I and II are low grade and grade III (benign) and IV are higher grade (malignant). Glioblastoma Multiforme is the most common type of glioma. Meningiomas derive from meningotheial cells and comprise about 20% of primary brain tumors.

Here is a quick overview of these tumors:

2.6.1 GLIAL TUMORS

- Astrocytoma: An Astrocytoma develops from star-shaped glial cells that support the nerve cells. These tumors can be located anywhere in the brain, but the most common location is in the frontal lobe. Astrocytomas are Grade III glioma tumors (Sheline, 1977).
- Brain stem glioma: It is named for its location at the base of the brain. Can range from low grade to high grade (Armstrong *et al.*, 2004). Brain stem gliomas are rare and poorly understood. Mean age onset is 34 years (Guillamo, 2001).
- Ependymoma: Ependymomas (EP) originate from ependymal cells of the wall of the cerebral ventricles, central canal of the spinal cord, and from ependymal remnants in the filumterminale, the choroid plexus or the white matter adjacent to the highly angulated ventricular surface (Combs *et al.*, 2006).
- Mixed gliomas: A mixed glioma is often a combination of an Astrocytoma and an Oligodendroglioma. This means that the tumor consist out of more than one type of glial cell (Armstrong *et al.*, 2004).
- Oligodendroglioma: An oligodendroglioma are well-differentiated, diffusely infiltrated tumor of adults that is typically located in the cerebral hemisphere (Peretti *et al.*, 2008).

- Optic nerve gliomas: Named for its location on or near the nerve pathways between the eyes and the brain. (Armstrong *et al.*, 2004).
- Subependymoma: This tumor forms from ependymal cells, and is a variation of an Ependymoma. Usually located in the fourth and lateral ventricles. More common in men than in women (Armstrong *et al.*, 2004).

2.6.2 NON-GLIAL TUMORS

- Acoustic neuroma: An *acoustic* neuroma, sometimes called a *vestibular schwannoma* is a benign tumor that is located on the 8th cranial nerve which leads from the inner ear to the brain (Medifocus, 2011).
- Chordoma: Occurs at the sacrum, near the lower tip of the spine or the base of the skull (Armstrong *et al.*, 2004).
- CNS lymphoma: develops in the lymphatic system. The lymphatic system is a network of small organs called the lymph nodes and vessels that carry clear, watery fluid called lymph throughout the body. Often develops in the brain, commonly in the areas adjacent the ventricles. This tumor is very aggressive (Armstrong *et al.*, 2004). Primary central nervous system lymphoma (PCNSL) is an uncommon extranodal non-Hodgkin lymphoma (Bhagavathi & Wilson, 2009). This tumor has been increasing in countries like the United States, and they typically occurs in patients with immunodeficiency syndromes (Chandana *et al.*, 2008).
- Craniopharyngioma: Most common in the parasellar region, an area at the base of the brain and near the optic nerves (Armstrong *et al.*, 2004).
- Hemangioblastoma: Commonly located in the cerebellum and originates from blood vessels (Armstrong *et al.*, 2004).
- Medulloblastoma: Medulloblastoma is highly malignant tumor in children and account for 10-20% of CNS neoplasms and approximately 40% of posterior fossa tumors (MacDonald & Packer, 2009). This tumor is unusually in adults. PNET/medulloblastoma refers to the posterior fossa in most adult patients (Peterson & Walker, 1995).

- Meningioma: Tumors grow from the meninges, the layers of tissue covering the brain and the spinal cord. This tumor may arise from previous treatment from ionizing radiation or excessive x-ray exposure (Armstrong *et al.*, 2004).
- Pineal tumor: A malignant tumor of pineal tumor called pineoblastoma. Named for its location in or around the pineal gland (near the centre of the brain). Can produce an excess of melatonin, a hormone that controls the sleep/wake cycle and can also block the ventricles causing hydrocephalus (Armstrong *et al.*, 2004).
- Pituitary tumor: Pituitary tumors are commonly encountered benign monoclonal adenomas that arise from cells of the anterior pituitary gland, accounting for approximately 15% of all diagnosed intracranial tumors (Chen *et al.*, 2011).

2.7 TREATMENT OF BRAIN TUMORS AND THE EFFECTS ON THE PATIENT

Treating cancer can be extremely difficult due to all cancer cells not behaving in the same way. Especially higher grade primary tumors like Glioblastoma Multiforme (GBM) are still one of the most challenging problems in neuro-oncology (Nakagawa *et al.*, 1998). By the time a cancerous tumor has been detected, it may contain a diverse population of cells. Some cells in this tumor will react to drugs and others would not, and some cells will metastasize and others would not, and some will divide where others would not (Schneider *et al.*, 2003). The fact also remains that the approach to treatment of Glioblastoma Multiforme or any primary brain tumor for that matter, varies from center to center (Durmaz *et al.*, 1997). Various approaches have been tried; most commonly a combination of surgical resection followed by radiotherapy with or without chemotherapy, few studies reported improvement of the result of treatment (Nakagawa *et al.*, 1997). Interstitial brachytherapy, radiotherapy, intraoperative radiation therapy (IORT), hyperthermia, and novel chemotherapy have been used to try and improve the outcome (Nakagawa *et al.*, 1997). Postoperative radiotherapy has been shown to improve local control rates and prolong survival for GBM when compared with surgery alone (Nakagawa *et al.*, 1997).

Surgery or resection is the primary form of treatment for brain tumors. The goal for surgery is to remove the tumor without causing damage to critical neurological functions.

Successful management of patients under a brain operation or for matter like brain injuries relies on clear understanding of physiological mechanisms and of the added effect of anaesthesia and manipulation of arterial pressure, CO₂ and O₂ tensions. Poor anaesthetic technique which allows coughing, straining, hypotension, exaggerated hypertension, hypoxia and hypercarbia will seriously damage the brain (Walters, 1998). Accurate preoperative localization of eloquent cortex enables optimal neurosurgical tumor resection and minimizes postoperative neurological deficits (Zhang *et al.*, 2009).

When only a part of the tumor can be removed, it is possible that the tumor will recur. So in most cases, if it is possible, the whole tumor must be removed. If only part of this tumor can be removed, it can alleviate the patient's symptoms as well as help with adjuvant therapies (Armstrong *et al.*, 2004). The radical tumor resection treatment has been getting a lot of attention, especially for high-grade brain tumors like GBM. Some authors have not supported this treatment due to the fact of accessing locations in the brain that is very deep localized. On the contrary, there have been reports that this type of treatment revealed a prolonged survival time and improve quality of life in patients with higher grade gliomas (Durmaz *et al.*, 1997). The question: what will be the best option, total resection or a biopsy? This decision will have an effect on the prognosis of the patient (Durmaz *et al.*, 1997).

There are two other standard types of treatments for patients with brain tumors namely radiation therapy and chemotherapy (Henson, 2005). If the tumor was diagnosed as Grade III or IV, the treatment for these patients starts as soon as feasible. The reason for this is in order for the patients to heal from the surgery. This usually means that the treatment of radiation therapy and chemotherapy will start within 2-4 weeks after surgery (Henson, 2005). If a patient decides to have a second opinion about his or her diagnosis, they must do it as soon as possible so that it will not delay the treatment process (Armstrong *et al.*, 2004).

Brain tumors, which are characterized by progressive impairments of mental function, a beneficial treatment may be one that stabilizes or slows the progression of worsening symptoms, whether or not overall survival is extended (Meyers & Hess, 2003). This is the main reason why treatment cannot be delayed in any way.

Members of the Food and Drug administration, the National Cancer Institution in the US (NCI) and the NCI Division of Cancer Treatment Board of Scientific Counselors, net clinical benefit of cancer therapy includes the following:

- a) Survival benefit;
- b) Time to treatment failure and disease-free survival;
- c) Complete response rate;
- d) Response rate; and
- e) Beneficial effects on disease-related symptoms and/ or quality of life (O'Shaughnessy *et al.*, 1991 In: Meyers & Hess, 2003).

Brain dysfunction caused by brain tumors is manifested by neurologic and cognitive impairment. Impairments due to the tumor itself are related to the site of the lesion and thus vary among individuals, according to Scheibel *et al.* (1996) In: Meyers and Hess, (2003). Treatment of these patients, particularly radiation therapy, tends to affect the subcortical white matter, causing impairment in cognitive speed, frontal lobe executive functions, memory, sustained attention, and motor coordination (Meyers & Hess, 2003).

The WHO (In: Kober, 2010) has proposed the following about clarifying the effects of neurologic disease on the patient with a brain tumor:

- 1) Impairment is the effect of the disease process on function of the brain, which is assessed by neurologic and neurocognitive evaluations;
- 2) Disability refers to the effect of the impairment on the patient's ability to function; and
- 3) Handicap refers to the impact of the impairment and disability on the patient's function in social and vocational roles and on life satisfaction.

2.8 QUALITY OF LIFE AND THE BRAIN TUMOR PATIENT

According to the Rayson and Reyno (2003), they saw an explosion of interest in the measurement of quality of life in patients with solid tumors receiving both adjuvant and palliative therapies. Most trials measured the QoL of the patient associated with therapeutic intervention. To sustain *quality of life* is the main aim for any brain tumor patient. Quality of life assessments in neuro-oncology are becoming more relevant with the proliferation of intensive research into brain tumors and their therapy (Bampoe *et al.*, 1998). All types of research data on Cancer and QoL will effectively help to better future intervention. As stated by Liu *et al.* (2008), quality of life is a concept that encompasses the multidimensional well-being of a person and reflects an individual's overall satisfaction with life. Quality of life will include ADL's, self-assistance, and independence as much as possible. ADL's will then include emotional-, functional-, physical- and social well-being (Liu *et al.*, 2008). The brain tumor patient will have a lot to adapt to in the beginning of the diagnosis and this may have a significant impact on their QoL from there onwards. How to manage the problem of adaption to diagnosis of a brain tumor, have not been addressed in studies in a very satisfactory manner as yet. It is important to note that the research of the QoL of these patient lack validated instruments for measurements. The only instrument that is currently used is the KPS scores. KPS generally correlates with the QoL of patients (Liu *et al.*, 2008) and the World Health Organization clinical performance status (Bampoe *et al.*, 1998). So there are a lot of challenges to overcome in this area.

Primary brain tumor patients face serious challenges in QoL. Patients with high-grade tumors do not appear to differ in QoL between those with grade III of grade IV tumors, although perceived QoL in patients with Grade III tumors may be better (Liu *et al.*, 2008).

Common knowledge will tell me that the lower the QoL of a newly diagnosed brain tumor patient is, the quicker there health will deteriorate. Psychological and/or emotional response plays a role in the side-effects as well as the quality of life of any cancer patient. The response included the pre-treatment, post-treatment and diagnosis responses. Studies suggested that characteristics of patients, such as anxiety and

coping style, might influence the development of conditioned chemotherapy side effects. Studies have shown that the patient that is informed about their condition reacts better and has less distress to the patient that shows fear-avoidance about their condition (Lerman *et al.*, 1990).

Certain symptoms that affect the QoL in primary brain tumor patients are usually sleep, pain, seizures, mood disturbance, and cognitive functioning. The most disturbing one that interference with QoL and ADL's, as already described earlier in the cancer section is *fatigue*. The occurrence of fatigue or CRF is more significant in the higher-grade gliomas than in low-grade tumors. Fatigue occurs in 89-94% of recurrent malignant gliomas (Liu *et al.*, 2008).

The different symptoms that burden the primary brain tumor patient's quality of life has not significantly been explored and researched. Of all the QoL interventions not many have been tested on brain tumor patients. The most researched and widely studied are fatigue and cognitive functioning (Liu *et al.*, 2008). According to Liu *et al.* (2008), non-pharmacological interventions like exercise are thought to potentially improve QoL outcomes.

2.9 OCCURRENCE AND PROGNOSIS OF PRIMARY BRAIN TUMORS

Due to the fact that survival rate outcomes from brain cancer are relatively poor, with only a 19% survival of the disease for five years or more. There has been no improvement in survival in the period since cancer registration began (Cancer Council South Australia, 2006). Although in the last 20 years we had seen advances in the treatment of and outcomes of brain tumor patients. This includes refined forms of surgical techniques, introduction of new chemotherapeutic as well as radiotherapeutic regimens and trials of biological therapies (Janda *et al.*, 2007).

Primary malignant brain tumors (cancer) are characterized by short-term survival and significant morbidity as the disease progresses (Meyers & Hess, 2003). Glioblastoma Multiforme (Grade IV) accounts for 27% of primary brain tumors, and the mean survival

time still is highly unsatisfactory, although there are some cases of long-term survival reported (Durmaz *et al.*, 1997). Secer *et al.* (2008) reported a median survival rate of 18.8 months. Studies done by Nakagawa (1997) noted that patients carrying this tumor have a poor prognosis, with a reported median survival time of less than 1 year from the diagnosis. Although, there was a study with a patient aged 16 that survived for 24 months, however the patient had a recurrence called “butterfly” at the primary lesion and died not long after that. A study by Durmaz *et al.* (1997) reported a local recurrence of GBM is inevitable after a median survival rate of 32-36 weeks. Durmaz *et al.* (1997) also revealed in their study after testing 46 patients with GBM and concluded that the overall median survival was 53 weeks which was a 95% confidence interval and then 41% of patients survived over a year and 8,6% over 2 years. With Anaplastic Astrocytoma, according to Levin *et al.* (2006), the patients’ had a median survival rate of 3 years. The prognosis of patients with Anaplastic oligoastrocytomas (AOA) is poor. After surgery and other adjuvant therapies like radiotherapy, the reported median survival time ranges from 2.8 – 5.8 years. Similarly, the median time to tumor recurrence was observed to be 4.5 years (Martinez *et al.*, 2005). Age does have an advantage in the case of a brain tumor diagnosis. A younger patient’s prognosis is much better than that of an older person (Scoccianti *et al.*, 2010).

With all of the above mentioned studies and theories it can be seen, that not one study’s outcome is the same. This will account for the specific type of tests that have been done on the patients, the way of diagnosis, the type of treatment and the amount and frequency of treatment (e.g. radiation therapy and chemotherapy). Barnholtz-Sloan *et al.* (1997) found that the aspect of race also have an influence on individuals diagnosed with a primary malignant brain tumor.

Patients diagnosed with primary brain tumor like an AA or GBM’s median survival rates or prognosis, as seen, still remain very poor and there is an obvious need for the development of more effective modalities with novel mechanisms of action and highlights the need for other measures of patient outcome, including ability to function and quality of life (Meyer & Hess, 2003; Watanabe *et al.*, 2005).

2.10 STATISTICS OF BRAIN TUMORS

According to statements of the National Cancer Registry (NCR), brain tumors are one of the top five cancer diagnoses under males and females in South Africa (Molete, 1999), but according to the American Cancer Society primary brain tumors falls among the top 10 causes of cancer related deaths (Armstrong *et al.*, 2004), which I believe will be the same for South Africa in the last year. In the United States 43 500 patients were diagnosed with malignant primary brain tumors in 2008 whereas 45% were gliomas, meaning higher grade or grade III-IV (Minn *et al.*, In: Bernstein & Berger, 2008). Primary brain tumors account for 2% of all cancer in United States' adult population (Chandana *et al.*, 2008).

According to Dr. Meyer, Neurologist at the Unitas Hospital in Centurion, Pretoria, and the statistics shows an upward and downward movement of diagnoses of brain tumors during the years. There are no specific times that the prevalence can be specified and why (Meyer, 2011).

The American Cancer Society estimates that there are more than 18,000 new diagnoses of brain and nervous system cancers causing more than 12,000 deaths each year in the United States. Data from the Surveillance, Epidemiology and End Results program showed an age-adjusted incidence of 6.4 per 100,000 person-year in 2003 compared to the 5.85 per 100,000 person-years in 1975 (Chandana *et al.*, 2008) There was a dramatic increase in brain tumor diagnoses in the last three decades. Cases of Glioblastoma Multiforme (GBM), which is a higher grade primary tumor, with lesions in unusual age groups and unusual sites are increasing in frequency (Sarsilmaz *et al.*, 2010), and most studies in developed countries show that the number of people who develop brain tumors and die from them has increased by some 300% over this period of time among childhood brain tumors and 75 year or older. There are no reasons stated to know how these people get or develop a brain tumor as of yet (Wrench, 2008). If the rate of diagnosis of brain tumors in developed countries has increased so much, the rate in undeveloped countries must have been worse. This would seem to indicate that the difference is due to better diagnosis and treatment in the developed countries

(Armstrong *et al.*, 2004). The average age that an adult is diagnosed with a brain tumor is 54 years. The age and number of children diagnosed with brain tumors is distributed evenly between ages 0 and 19. Statistics shows that children deaths due to primary brain tumors are one quarter of all cancer deaths (Wrench, 2008). Findings of recent studies suggest that female hormones may have a protective effect against certain types of brain tumors. Tumors in cranial and spinal nerves and in the cellar region of the brain (the area just behind the eyes) occur equally in males and females (Armstrong *et al.*, 2004).

2.11 EXERCISE INTERVENTION AND THE HUMAN BRAIN

The word “exercise” derives from a Latin root meaning “to maintain”, “to keep”, “and to ward off” (Kramer, 2003). This is the main purpose of this study is to maintain quality of life. Maintaining brain health and plasticity throughout life is an important public health goal, and it is increasingly clear that behavioral stimulation and exercise can help us to achieve it (Cotman & Berchtold, 2002).

2.11.1 Processes in the brain during exercise

What goes on inside your brain when you exercise? How exactly exercise affects the staggeringly intricate workings of the brain at a cellular level has remained largely mysterious. Although there are said that exercise is a powerful tool to simulate several brain processes, and it is becoming clear that therapeutic effects of exercise are not only good for cardiovascular and other diseases, but importantly it is good for your brain (Meeusen, 2005).

According to a survey done from existing researched published by the Cochrane Library in 2010, aerobic exercise is good for your heart and also improves cognitive function – specifically motor function, auditory attention, memory in healthy older adults (Hobson, 2008). Physical activity, such as walking or running on a treadmill, swimming, and weight-bearing exercise, is known to increase neural activity in both peripheral and central nervous system (Seo *et al.*, 2010). Especially walking is good for your brain, because it increases blood circulation and the oxygen and glucose that reach your brain.

Walking is not strenuous, so your leg muscles don't take up extra oxygen and glucose like other types of exercise. As you walk, you effectively oxygenate your brain. Studies do show that in response to exercise; cerebral blood vessels can grow. Stroke risk was cut by 57% in people who walked as little as 20 minutes a day (Kramer, 2003).

All forms of exercise can increase your blood circulation, independence level, musculoskeletal strength and flexibility and cardiovascular functioning capabilities (Welsh, 2010).

2.11.2 Mind-body connection through exercise

You may have heard about the term “mind-body connection”? Did you know that there is actually a physical connection between the brain and the muscles? This is called the neuromuscular junction (Kramer, 2003). Brain chemistry reveals an essential unity of mind and body. At the neuromuscular junctions the brain uses acetylcholine – its primary chemical neurotransmitter for memory and attention – to communicate with muscles. Another brain's key chemical messengers, dopamine, helps regulate the fine motor movement. The role of these neurotransmitters in regulating movement underscores the intimate relation between body and mind, muscle and memory (Kramer, 2003).

Many scientists in the field want to find out the answers to the question on how exercise remodels the brain (Reynolds, 2010). Brain scans confirm benefits of physical exercise. Exercise is essential for preserving brain function for everyone. Kramer (2003) explains how it works: muscles activate brain receptors. When acetylcholine is released at a neuromuscular junction, it crosses the synapse that separates the nerve from the muscle. It binds to the acetylcholine receptor molecules that initiate a chain of events that lead to muscle contraction.

Studies done by Lichtman & Sanes (2003), at Washington University in Neurobiology, showed that a loss of nerve signals – due to inactivity – actually disassembles this scaffold and causes a loss of acetylcholine receptors. The scaffolds plays a role in

tightening its grip to acetylcholine receptors, therefore it is important to be active. If you regain activity the scaffolds will tighten its grip and catch any receptors that comes by, therefore you get those receptors back (Lichtman & Sanes, 2003).

2.11.3 Neurogenesis and exercise

According to Arthur Kramer, exercise leads to brain benefits and is therefore confirmed for humans. His findings provided that the first empirical confirmation of the relationship between cardiovascular fitness and neural degeneration as predicted in various academic studies on aging and cognition in the human population (Kramer, 1970). Dr. Fred Gage and his colleagues at the Laboratory of Genetics at the Salk Institute in San Diego proved that human and animal brains produce new cells namely neurogenesis even in the ageing brain (Covalt, 2006; Reynolds, 2010).

Scientists at Feinberg School of Medicine of Chicago have manipulated the levels of *bone-morphogenetic protein* (BMP) in the brains of laboratory mice. BMP is found throughout the body, affects cellular development in various ways, some of them deleterious. In the brain BMP has been found to contribute to the control of stem cell divisions (Reynolds, 2010).

According to these scientists, they say that your brain will be very pleased to know that if it is packed with adult stem cells, which given the right impetus, divide and differentiate into either additional stem cells or baby neurons. With age, these stem cells in the brain tend to become less responsive and do not divide as readily and can slump into a kind of a cellular sleep, according to Dr. Jack Kessler the chairperson of Neurology of Northwestern University. This cellular sleep will initiate if the person is either inactive by means of exercise or cognitive work. The more active BMP and its various signals are in your brain, the more inactive your stem cells become and less neurogenesis you undergo. Your brain grows slower, less nimble and older (Reynolds, 2010). With exercise countermands some of the numbing effects of BMP and exercise showed a notable increase in *Noggin*, a brain protein that acts as a BMP antagonist. The more *Noggin* in your brain, the less BMP activity exists and the more brain stem cell divisions

and neurogenesis you experience (Reynolds, 2010). So this proves that human brain can continue to grow and improve with exercise (Kramer, 1970).

2.11.4 Exercise-releasing natural chemicals that enhance brain health

Exercise modulates both plasticity and various supporting systems that participate in maintaining brain function and health (Cotman *et al.*, 2007). Brain health is important in a lot of aspects of the overall health of the human body. A lot of negative impacts may arise from negligence of the human brain or for our arguments' sake, the absence of exercise. Illness like depression and stress are only two of these negative impacts of the absence of no exercise.

Beta-endorphin may be the natural mood-enhancing chemical that may be the key player in the ability of exercise to protect the brain against aging! An international team also found that beta-endorphin, produced by the hypothalamus and the pituitary gland, may be a key factor in the beneficial effects of exercise on the brain (Covalt, 2006). According to Gómez-Pinilla *et al.* (2006) of the University of California did studies on animals showed that exercise could help regenerating a damaged brain circuits. Studies in Atlanta done by Gómez-Pinilla *et al.* (2006) found that exercise reduces the inhibitory capacity of the injured brain and thus may help reverse some of the devastating consequences of traumatic brain injury They also found that exercise reduces the inhibitory capacity of the injured brain and thus may help reverse some of the devastating consequences of traumatic brain injury. Human and other animal studies demonstrated that exercise targets many aspects of brain function and has broad effects on overall brain health, including neurogenesis, CNS metabolism and angiogenesis (Cotman *et al.*, 2007).

If a the brain is injured in some way, it reduces the levels of the production of *Protein kinase A* (PKA), a brain chemical that enhances the protective effects of *Brain Deprived Neurotrophic Factor* (BDNF) (Covalt, 2006).

Abundant evidence from animals and human research supports the idea that BDNF is essential for hippocampal function, synaptic plasticity, learning, and modulation of depression. Exercise does increase BDNF in several brain regions, and the most robust and enduring response occurs in the hippocampus (Cotman *et al.*, 2007). Exercise does increase BDNF in several brain regions, and the most robust and enduring response occurs in the hippocampus (Cotman *et al.*, 2007). Research done by Gómez-Pinilla and colleagues again demonstrated that involved brain-injured rats, voluntary exercise increases the levels of BDNF, a protein that is crucial for growth of neurons and for brain processes involved in learning and memory (Covalt, 2006).

The notion of improvement of learning and memory due to exercise intervention has been verified by another study that found that the benefits of exercise has also been defined for protection from neurodegeneration and alleviate of depression, particularly in elderly population. Exercise also increases synaptic plasticity of directly affecting synaptic strength, and by strengthening the underlying systems that support plasticity including neurogenesis, metabolism and vascular function (Cotman *et al.*, 2007).

Exercise reduced, post-trauma increase the levels of two other proteins, *Myelin-Associated Glycoprotein* (MAG) and *Nogo-A*, which inhibit the growth of new axons, the nerve cell fibers that send electrical impulses to other neurons (Covalt, 2006). By reducing levels of proteins that inhibit new neural growth and by increasing levels of the protein that enhances such growth. This opens the possibility of harnessing this capacity of exercise to promote neural healing (Covalt, 2006).

Smeyne *et al.* (2006) found cell-destroying neurotoxins in the brain and that showed evidence that exercise must be changing something in the cell itself than rather than simply altering the toxin's metabolism (Covalt, 2006). Exercise and the role that different chemicals play in the brain has an overall change in the human body for instance. There are a lot of changes happening only in the brain that may help or prevent different life threatening diseases or illnesses. A key mechanism mediating these broad benefits of exercise on the brain is induction of central and peripheral growth factors and growth

factors cascades, which instruct downstream structural and functional change (Cotman *et al.*, 2007). Therefore this means that chemicals in the brain will be expressed differently in certain situations.

The findings from these studies suggest that at least two months of exercise are needed to protect the cells and that higher levels of exercise were significantly more beneficial than lower amounts, although all exercise was better than none! They also found that three months of sustained exercise significantly altered the expression of numerous proteins in the brain, including ones that help move molecules in and out of cells and that control different gene expression (Covalt, 2006).

2.12 EXERCISE, THE BRAIN AND DIFFERENT SYSTEMS

2.12.1 Chemical regulators

Chemicals influenced by exercise, including neurotransmitters and growth factors are being investigated for the role they play in brain function and other possible factors it may influence. A number of studies have examined brain *noradrenaline* (NA), *serotonin* (5-HT) and *dopamine* (DA) with exercise (Covalt, 2006). They found that physical exercise influences the central *dopaminergic*, *noradrenergic* and *serotonergic* systems.

A study was done in Germany on 10 athletes where they used PET scans to look at these athletes brains following a two-hour run. The scans confirmed that during run, *endorphins* were released in certain parts of the brain known to be involved with the processing of emotions. The endorphins usually cause “runners’ high”, but it is not the sole regulators of mood and emotions during a workout (Hobson, 2008). Emotional feeling plays an important role in exercise. It is a mood enhancer, like we saw with the study that was done of Germany on the athletes and this is just one of these types of studies. Endorphins are just one of these mood enhancing chemicals that contribute to the emotional well-being of any person, but so are *norepinephrine*, *serotonin*, *dopamine*, and *brain-derived neurotropic factor* (BDNF) (Hobson, 2008).

2.12.2 Brain Deprived Neurotrophic Factor (BDNF)

BDNF is a molecule that helps support the survival of existing neurons and encourage the growth of new neurons. In the brain, it is active in the hippocampus, cortex, and basal forebrain (Anon, 2010).

Due to the difficulty of measurement of BDNF, the understanding of BDNF protein is not quite as well understood as we need to, even though a wide variety of studies of BDNF mRNA have been done in the past (Nawa *et al.*, 2006)

Among various neurotrophic factors, BDNF is well-known not only to increase neuronal survival and plasticity, but also to exert a protective effect on brain diseases, such as stroke, ischemia and trauma (Seo *et al.*, 2010).

BDNF is known to increase with exercise. This increase is believed to originate from the brain and it is suggested that monoamines are involved in BDNF regulation. In a study that was done where animal models were used for voluntary wheel-running, it was found that there was an increase levels of BDNF mRNA in the hippocampus, a highly plastic structure that is normally associated with higher cognitive function than motor activity (Goekint *et al.*, 2011). In a study done by Stranahan *et al.* (2009) it was shown that running-wheel activity, caloric restriction, or the combination of the two treatments increased levels of BDNF in the hippocampus of diabetic mice. Research in humans, therefore, suggests that exercise and behavioral stimulation can maintain or improve brain plasticity. Learning, a higher order of brain plasticity, increases BDNF gene expression, and BDNF, in turn, facilitates learning (Cotman & Berchtold, 2002).

When exercising, energy from sources like glucose and carbohydrates are needed. In this case BDNF levels in the hippocampus are responsive to alterations in glucose levels (Anson *et al.*, 2003; Duan *et al.*, 2003 In: Stranahan, 2009), and BDNF plays a role in the cellular metabolism (Burkhalter *et al.*, 2003; Yeo *et al.*, 2004 In: Stranahan, 2009). As we all know that cellular metabolism controls the way the body use and produce energy to sustain life.

There is also evidence that BDNF expression may be a downstream target of monoamines-enhancing, mood-stabilizing antidepressant treatments and could be an important agent for therapeutic recovery from depression and the protection against stress-induced neuronal damage (Garza *et al.*, 2003). In addition to BDNF, it is remarkable that exercise regulates the expression of so many genes in the hippocampus, and the findings underscores the emerging idea that exercise is a powerful effector of brain physiology (Cotman & Berchtold, 2002).

2.12.3 Cerebrospinal blood flow (CBF) and serotonin (5HT)

Cerebrospinal blood flow must be maintained to ensure a constant delivery of oxygen and glucose as well as the removal of “waste” products. Maintenance of cerebral blood flow depends on a balance between the pressure within the skull, intracranial pressure (ICP) and the arterial pressure of the blood, mean arterial pressure (MAP) (Walters, 1998).

Exercise increase the brain's capillary bed and elevates *cerebral blood flow* (CBF) which, in turn, serves to help protect against the extensive damage that normally occurs following brain damage like a stroke. The above statement proved an approximate 35% improvement in brain blood flow subsequent to stroke over that of the control animals in a study done by Davis (Covalt, 2006). The results indicate that there is evidence in favor of changes in synthesis and metabolism of monoamines and serotonin during exercise in a study done by Dey *et al.* (1992). Serotonin is critical in many brain functions, including the regulation of mood, heart rate, sleep, appetite, pain and many others. As a result, it is extremely important that the neuron release the proper amount at the right time (Senerth, 2002). When Serotonin is released into the synapse between the neurons, it comes in contact with receptors on the dendrite of another cell. From all the receptors, its cell body decides whether or not to fire an electrical impulse down its own axon. If a certain amount of receptors binding occurs, the axon will fire, causing the release of neurotransmitter into the synapses of other cells (Senerth, 2002). This is how the brain cells communicate and regulate the amount of neurotransmitters present at any given time. Research has shown that the amount of serotonin receptors binding

influences your mood. When more receptors are active, you are happier (Senerth, 2002).

Serotonin is necessary for short-term modulation of the exercise ventilator response. Tryptophan, also a protein that is necessary for the forming of serotonin in the brain. Serotonin is made from the amino acid L-Tryptophan by hormone-producing enterochromaffin cells in the gut and airways of the lung (bronchi). Serotonin opens up (dilates) blood vessels and causes clumping of platelets (platelet aggregation). It is broken down in the liver to 5-HIAA and later ends up in the urine (www.health24.co.za, 2006).

In the study by Dey *et al.* (1992), they tested acute and chronic exercise bouts with rats to see where the serotonin (5HT) accumulates during this exercise in 4 regions of the rats' brain. Alterations of 5HT and its chief metabolite 5HIAA were studied following 1-hour of exercise and 4 week chronic exercise (30 minutes/day, 6 days a week). Acute exercise significantly increased the synthesis and metabolism of 5HT in the brain stem. Hypothalamus also showed increased levels of 5HT. However, no changes were observed in the cerebral cortex and hippocampus during acute exercise. Chronic exercise activated not only the synthesis but also the metabolism of 5HT in the cerebral cortex; this neuronal adaptation was sustained even 1 week after the termination of training.

Brain 5HT has been suggested to be involved in CNS fatigue during prolonged exercise which is one of the negative effects of 5HT. Good evidence have shown that the increasing and decreasing of 5HT can hasten and delay CNS fatigue during prolonged exercise (Davis & Bailey., 1997). Also increased 5HT in blood, cerebrospinal fluid and spinal cord have earlier been demonstrated in traumatic, ischemic and metabolic insult to the central nervous system. Therefore we can see that serotonin does play an important role in the functioning of the brain during exercise

2.12.4 Blood-Brain Barrier (BBB)

The BBB consists of capillary endothelial cells that lack fenestrations (openings), have low pinocytotic activity and high electrical resistance, and are connected by continuous tight junctions to keep undesirable agents from entering the brain. Most molecules that cross the BBB are small in molecular weight, non-polar, and hydrophobic, permitting diffusion through lipid bi-layer membranes. Due to the fact certain molecules that pass through the BBB for essential cerebral metabolic processes, this means that chemotherapeutics are actively transported out of the brain through the BBB by efflux carriers, thereby limiting the exposure of the CNS (Palmieri *et al.*, 2009). According to Steeg (2009), we need to find drugs that cross the BBB that normally protects the brain from most blood-borne molecules (Steeg *et al.*, 2009).

The BBB is the prime determinant of the brain's status as a chemotherapy sanctuary site for tumor cells. The invasion and colonization of a tumor cell that passes through the BBB may lead to the forming of a metastatic tumor. This progressive growing tumor opens the permeability of the blood brain barrier to create a blood-tumor barrier, but the evidence and data are still limited on this topic (Palmieri *et al.*, 2009).

Parkinson's and Alzheimer's disease are both connected with leakage through the BBB. The importance of the BBB, where it prevents certain substances to cross into the brain, it can cause preventing very important medication to enter the brain. *Vorinostat*, that is one of the drugs used in cancer, has been found to enter through the BBB and slow the growth of primary brain tumors of several different types of mice. Palmieri *et al.* (2009) said that there is a need to find agents to treat the central nervous system lesions and brain metastasis, or for that matter primary brain tumor lesions.

Throughout all the above statements with regards gene expressions, neurotrophic factors and different systems that positively influences the brain during exercise; it was Ratey that said that if you want these brain and emotional benefits, "some exercise is better than nothing!" (Hobson, 2008) Then Castell noted that a single 10-minute bout of physical activity in an academic setting boost attention and problem-solving skills in kids (Hobson, 2008) An article that was published in the British Journal of Sports Medicine

found that if you do the recommended 30-minute a day aerobic activity will cover your brain and your heart (Hobson, 2008).

A recent study from Ivanhoe Newswire believes that exercise can strengthen the BBB. In a study done by Medalie (2009) with mice, where they had two groups of 3-month-old mice, representing men in their 20's. Both groups were given the human equivalent of methamphetamine. The experimental group received exercise wheels and the control group did not receive exercise wheels. The meth usually increases body temperatures as well as cause agitation. The exercising mice got active, but on the other hand, the sedentary mice experienced increasing oxidative stress, affecting the permeability of the BBB. The exercising mice did not show any of these results (Medalie, 2009).

It is therefore remarkable that exercise regulates the expression of so many genes in the hippocampus, and the findings underscores the emerging idea that exercise is a powerful effector of brain physiology (Cotman & Berchtold, 2002).

2.12.5 Cardiorespiratory component and the brain

Cardiac output is the primary indicator of the functional capacity of the circulation to meet the demands of physical activity (McArdle *et al.*, 1994). Endurance exercises are usually the component used in targeting the cardiovascular system including the heart muscle and the lungs or in other words the "oxygen delivery system" (Schneider *et al.*, 2003). The effect of long-term endurance exercise intervention can be seen both in the resting state and during physical activity. In general, the heart muscle and associated vascular structure become stronger, improving the capacity to accept and deliver blood. In this case the prescription of aerobic exercise in the patients program, will help improving the resting heart rate of the patient and will therefore make the heart stronger (Schneider *et al.*, 2003). Blood flow increases in proportion to the intensity of exercise. In progressing from rest, like any new diagnosed brain tumor patient, a steady-rate exercise will lead to an increase cardiac output till it reaches it plateau where the blood flow will be sufficient for that type of exercise intensity and it will meet the metabolic requirements for that exercise session (McArdle *et al.*, 1994). The patient will then

gradually exercise the cardiac muscle to the point of handling a certain capacity of exercise in order for them to handle their ADL as sufficiently.

By strengthening the patient's cardiovascular system, the patient will therefore have lung function capacity that means no breathing problems; the heart muscle will become stronger and therefore pump more the oxygenated blood more efficiently to various part of the body and will optimize the function of the body. The stronger the heart muscle the larger the stroke volume which means the heart does not have to beat as often to produce the necessary cardiac output. This type of exercise also leads to a slight lowering in the diastolic and systolic blood pressure and an increase blood volume and production of red blood cells, with concomitant of hemoglobin concentration (Schneider *et al.*, 2003). All of the above physiological improvements of the human body may help lessening any other unnecessary complication of this disease.

In this type of programs endurance exercise just focus on the aerobic system and not working against very high loads that initiate muscle strengthening as well. If we look at what influence the aerobic type of exercise has on the cancer patient it is a well research conclusion that were reached, because it gives the patient a higher stroke volume of the heart, greater cardiac output, increased blood volume, and increased hemoglobin concentration, greater lung volume, increased diffusion capacity at rest and during exercise - all of which will improve the patient's functional capacity, making daily tasks more manageable (Schneider *et al.*, 2003).

2.13 EXERCISE INTERVENTION AND THE BRAIN TUMOR PATIENT

According the "do-it-yourself"-website patients with a full blown or advanced type of cancer, needs to focus on their physical fitness and maintain optimal health and wellness (Anon, 2010). Therefore according to Dr. Melinda Irwin, an expert on cancer and exercise at Yale University School of Medicine, exercise will become a target therapy that will be (2003) prescribed for cancer rehabilitation in the future (Washburn, 2008). Already in 2003, the Journal of Clinical Oncology published that there is a growing amount of literature on the effect of exercise on QoL of cancer patients (Rayson

& Reyno, 2003). It is now eight years later and the amount of research done on the association of exercise and cancer are growing rapidly.

It was stated earlier in this study is that most cancer therapies interfere with QoL and overall health of the cancer patient. It was also proven by researchers like Rayson and Reyno (2003).

New studies has shown that exercise improve mood and memory of a brain tumor patient after they have received radiation therapy. Exercise appears to prevent the decline of erasable memory, which is similar to the memory problems patients with brain tumors experience following whole brain radiation (www.ivanhoe.com, 2009). It is also a fact that physical activity such as walking or running on a treadmill, swimming, and weight-bearing exercises, is known to increase neuronal activity in both the peripheral and central nervous system (brain) (Seo *et al.*, 2010).

This new information of exercise intervention and bettering the brain tumor patient's QoL, help promote the previous studies done by Jones *et al.* (2007) of the Duke University in North Carolina in America where they started with studies surrounding the potential of using exercise as an adjuvant therapy for the management of brain cancer patients. They showed, through several systematic reviews and one meta-analysis, promising preliminary evidence of physiological and psychological efficacy of exercise during and following the definitive adjuvant therapy (Jones *et al.*, 2007). Exercise has also been well-established as an effective intervention to prevent, minimize, or decrease fatigue (Ingram & Visovsky, 2007).

Most preliminary studies for this type of intervention was mostly done on breast cancer patients, but there is some mounting evidence that this exercise intervention will be beneficial for a diverse range of malignancies that differ significantly in terms of clinical presentation, pathology and prognosis (Jones *et al.*, 2007).

The early pioneering work of MacVicar and Winningham regarding the effect of aerobic exercise on fatigue and functional ability, which have a huge influence on the ADL of a brain tumor patient, made a substantial contribution to our understanding of how exercise mitigates cancer-related fatigue. Winningham's proposed Psychobiologic Entropy Model based on the relationship between deconditioning and functional ability inspired a paradigm shift from rest to exercise as a fatigue intervention for cancer survivors (Ingram & Visovsky, 2007).

The statement of exercise intervention for cancer-related fatigue and other pathologies during the treatment means that it includes primary brain tumor patients according to Jones *et al.* (2007). Conventional brain tumor management is associated with a broad array of debilitating neurological and functional side-effects. The muscle wasting process, due to the long-term doses of glucocorticoid therapy that causes severe debilitation of the patient's functional status. This poor functional status of the patient affects his or her ability to exercise (Jones *et al.*, 2007).

2.13.1 Cancer-related fatigue and the brain tumor patient

Fatigue is also a common complaint among people who have been diagnosed and treated for different varieties of brain tumors. As previously explained in the cancer section on CBF, fatigue is defined as an energy deficit that, if persistent, leads to a cycle of decreased activity, fatigue, and reduced function, which according to Winningham, results in disability (Ream *et al.*, 2006). Patients affected by fatigue describe overwhelming feelings of exhaustion that interfere with their ability to carry out their daily activities (ADL) (Conn-Levin, 2005). It is the symptom that these patients did not expect and were not prepared for the experience of the fatigue (Molassiotis *et al.*, 2010).

Fatigue can manifest itself in various ways in a brain tumor patient. Some examples are physical-, social-, attentional-, spiritual- or emotional changes. The patient that experience fatigue needs to accept this as a valid medical condition. What the patient needs to pinpoint how does the fatigue impacts his or her own life and what worsen the feeling of fatigue. The question that is asked is how fatigue develops. Then there are

certain medical conditions like side effects from medication, anemia, insomnia, depression, dehydration, poor nutrition and chronic pain. A study done by Ream *et al.* (2006), aimed to enable patients to manage fatigue through energy conservation and management and to optimize activity and functioning.

The Psychobiological Entropy model proposes that interventions should aim to either reduce the onset of fatigue (i.e. address the factors giving rise to it, including this case the disease and chemotherapy administered) or prevent secondary fatigue through achieving an optimal balance between restorative rest and restorative energy (Ream *et al.*, 2006). Coping with fatigue reduce the burden on cancer patients' lives, and allow them to lead lives with better quality (Ream *et al.*, 2006).

2.13.2 Influence of exercise intervention on cancer-related symptoms including CRF

From the above information we can clearly see that using exercise intervention as an adjuvant therapy for primary brain tumor patients will be a challenge in a lot of areas. Although prior reports of have demonstrated that resistance and endurance exercise intervention can significantly reverse muscle muscles in non-cancer populations. There is consistent evidence across studies that exercise improves fatigue, physical fitness, and functional ability in cancer survivors (Ingram & Visovsky, 2007). According to a study done in Denmark that was published in the British Medical Journal in 2009, people with cancer that is under a supervised exercise program, will likely have less fatigue and a greater feeling of well-being during chemotherapy. Promising results have also been reported for weight maintenance, body composition, metabolism and immune function (Ingram & Visovsky, 2007). A study done by Jones *et al.* (2007) in the brain tumor population by means of a survey showed that these patients are very interested, feel capable and are motivated to engage in exercise intervention programs following their diagnosis.

Engaging in an exercise intervention program, Velthuis *et al.* (2009) found that a workload of 40% of maximal oxygen uptake (VO_2 max) can be sustained throughout the

day without premature fatigue. When normal physical capacity is reduced, the workload of normal physical activities demands a relatively higher percentage of physical capacity, resulting in premature fatigue. Physical exercise of sufficient frequency, intensity and duration improves physical capacity through increased cardiac output and increased capillarization, and increased number of mitochondria and mitochondrial activity in the periphery; thereby it may lead to a reduction in CRF (Velthuis *et al.*, 2009).

It is important to realize that studies have not specifically test or investigate the exercise intervention on primary brain cancer patients. All studies are only conclude on surveys or basically passed on other cancer survivors' behavior and preferences with regards exercise intervention. The theory that was used up to now to do all these studies is called the theory of planned behavior (TPB). This theory is used to understand the determinants of exercise behavior in cancer patients. TPB is a social cognitive model of expectancy value that postulates that behavioral intention is the proximal determinant of behavior.

2.13.3 Symptoms and intervention that influence ADL of primary brain tumor patients

Brain tumor patients are exposed to stress and fear and this can influence their brain and other systems in their bodies. Stress is defined as a physical and psychological challenge to normal homeostasis (Adlard & Cotman, 2003). Most patients are treated with antidepressants and anti-anxiety medication during their tumor based treatments. According to Cotman and Berchtold (2002) they found that prolonged exposure to stress hormones for example corticosteroids is harmful for neuronal health and survival, particularly in the hippocampus. In response to acute and chronic stress, neurons undergo morphological changes, including dendritic atrophy and spine reduction, which have a negative impact on brain plasticity.

Therefore, exercise where always believed to be a stress relieving strategy and therefore reduce depression and anxiety in humans (Cotman & Berchtold, 2002). Corticosteroids decrease BDNF availability in the hippocampus, although exercise

before a stressful event can counteract this down regulation. It was also found in a study in breast cancer patients that cancer treatments have adverse effects on the immune system. Animal and human studies have shown that endurance (aerobic) training can provide protection against cancer by increasing macrophage and natural killer-cell cytotoxic activity. The idea that exercise may enhance immunity in cancer survivors has been a focus of several investigations, but the results are equivocal (Ingram & Visovsky, 2007).

2.14 EXERCISE INTERVENTION FOR HIGH RISK OR CHRONIC ILLNESSES

Most critical illnesses affect patients' physical function. Historically, patients with chronic diseases were advised to rest and to avoid physical activity. Medical opinions however changed throughout the years towards the belief that patients should engage in physical activity or a rehabilitative exercise program.

Cardiology was the first medical specialty to incorporate exercise rehabilitation into their treatment protocol and evaluated it. If exercise intervention had shown 20 years ago that it will prevent fatal heart attacks, it would have been incorporated into the treatment protocol then. Therefore, nowadays, a 12-week exercise intervention is used for all cardiac patients and believes it will soon apply for any cancer patient too according to Dr. Irwin from Yale Medical University (Washburn, 2008).

The recommendation of exercise is usually prescribed by now by most medical professionals for all cancer patients or other chronic illnesses like high blood pressure, cholesterol etc., as an adjuvant therapy in their treatment protocol. Psychological, social and physical benefits of physical exercise after myocardial infarction, coronary bypass grafting; heart transplantation and stable congestive heart disease are well documented. According to this same study, exercise intervention has a positive influence on mild and moderate depression, as well as clinical depressed patients (Oldervoll *et al.*, 2003). Depression is just one of the many side effects for any cancer patient. The reason for this is that exercise has so many positive influences on the human body that it only can be an improvement on the patients' quality of life.

2.15 EXERCISE RECOMMENDATIONS FOR BRAIN TUMOR PATIENTS

The following recommendation will give list of how to approach the brain tumor patient during and after cancer treatment with regards exercise. In the domain of coping techniques, Molassiotis *et al.* (2010) note a heightened awareness of the need to psychological and physiological readjust to the diagnosis. Physical activity will help with the most troublesome symptom namely fatigue. Although we cannot expect that a brain tumor patient can exercise at the level and intensity of “normal” healthy guidelines, therefore rehabilitations parameters must be tested (Shipp *et al.*, 2006). The brain tumor patients are usually very fragile patients and in most cases need assistance when they exercise even if it is just for moral support. The purpose for this study and in most health professionals with the knowledge of this condition, is to strive to help the brain tumor patients to become more physical capable, active and stronger as much as possible, for the main purpose to of promoting the patients’ quality of life (Cancer Treatment Centers of America, 2008).

2.15.1 Positive influence of exercise on brain tumor patient

Exercise may help a cancer patient to cope in several ways according to Jefford *et al.* (2008):

- It can help you feel in charge of your life;
- It can increase your energy and reduce *fatigue*;
- For some people on chemotherapy, exercise can reduce nausea and vomiting;
- It can help digestion and reduce constipation;
- It can increase strength, flexibility and heart and lung function;
- It can improve your mood; and
- Improve self-confidence (Hoffman, 2010).

The potential of improving the lives of cancer survivors is currently one of the foremost areas of research in cancer control (Ingram & Visovsky, 2007). Evidence of the benefits of exercise for cancer survivors has mounted steadily over the past two decades particularly in the areas of psychological and quality of life outcomes and cancer-related fatigue. More recently, improvements in physical functioning, body weight and body

composition, muscle strength, endurance and immune function have been reported (Ingram & Visovsky, 2007). For all of these reasons of improving the well-being of cancer survivors all of the above aspects may also be improved by exercise in the brain cancer population. There is growing evidence to suggest that regular exercise after a cancer diagnosis can reduce the chance of the cancer coming back (Hoffman, 2010).

A study that was conducted among the cancer population to prove the theory of the influence of exercise on the patient's health, the participants had to follow a 4-week moderate and home-based exercise program. After these 4-week training, the exercise group were doing more than 10,000 steps recommended for healthy people (Cancer Research UK, 2009). Another study that was implemented among cancer patients that was under intensive treatment. The patients that were exercising were fitter at the end of the study and made fewer complaints about fatigue. So according to the Cancer Research in the UK, having cancer you need NOT stop exercising (Cancer Research UK, 2009). So in this regard, exercise will therefore improve the ADL of patients that has been diagnosed with most type of cancers including brain tumors/cancer.

In studies done by Courneya *et al.* (2003) and Segal *et al.* (2001) they confirmed that randomized controlled trials with structured interventions targeting exercise among patients completing adjuvant therapy or during palliative hormonal therapy can be accomplished.

2.15.2 Exercise recommendations during or after cancer treatment for brain tumor patients

Studies show that after a cancer diagnosis, patients tend to slow down Stress, depression and feeling sick or fatigued from cancer treatment all tend to make them less active (Hoffman, 2010). Therefore it is important in the case of exercise recommendations for the brain tumor patient, to try maintaining some level of physical activity. Exercise, even minimal physical exertion, increase heart rate and muscle flexion, while boosting the body's tolerance to conventional brain cancer treatment (Cancer Treatment Centers of America, 2008).

A meta-analysis done by Velthuis *et al.* (2009) provides evidence that exercise is beneficial in the management of the most problematic symptom named CRF, also during cancer treatment. This meta-analysis included studies during or after cancer treatment describing adults of any age, regardless of gender, tumor type, tumor stage and type of cancer treatment. Interventions could take place in any setting and all types of exercises are included (Velthuis *et al.*, 2009).

The type of exercises required for the brain tumor patient to engaged in, it is important and critical that the program that is prescribed according to the patient's age, baseline fitness levels, and exercise experience (Ingram & Visovsky, 2007). Another important factor to consider before prescribing exercise intervention to a brain tumor patient will be the stage of the cancer that it is in, the medical treatment they are undergoing and other co-morbidities. All of the correct exercises appears to be a safe and well-tolerated adjunct to treatment when appropriately taught and monitored, and is viable intervention to reverse or prevent the negative effects of cancer treatment on physiologic outcomes (Ingram & Visovsky, 2007).

Exercise rehabilitation during or after treatment is now considered an effective means of restoring physical and psychological health for the brain tumor patient during and after cancer therapy. It is very important to consider the way of how to approach the exercise intervention accordingly. If the patient is in treatment (or have recently finished) it is fine to exercise if you feel like it, but it is important to not overdo it (Cancer Research UK, 2009). To prevent overdoing or not doing exercise, it will be the best for an Exercise Specialist/Biokineticist or Physiotherapist to help with the correct way of approach of treatment for these patients. It is important to advise cancer survivors to exercise within their tolerance limits, provided that they receive and adequate health assessment and has no contraindications to engaging in physical activity based on co-morbid health conditions (Ingram & Visovsky, 2007).

For people who were active before the cancer was diagnosed, it is a good idea to stay with exercises they are familiar with. People who used to exercise vigorously may need

to do less, especially if their fitness has reduced due to bed rest after the diagnosis as well as start of the cancer therapy protocol (Jefford *et al.*, 2008). Due to the fatigue that is the most common symptom of the cancer therapy that the patient's usually is trouble with, the patient must not force his or herself to exercise if they don't feel like it, especially for the brain tumor patient. Just moving around is already purposeful for the patient (Jefford *et al.*, 2008). The patient must not think that they need to work up a sweat or train for a marathon to obtain the benefit of the exercise, according to Dr. Irwin from Yale Medical University (Washburn, 2008). Let them take it slow, by means of just walking in the garden or walking from bedroom to the kitchen or living room to the kitchen. This means that the patient is building an exercise program into their daily lives. Therefore the patient does not even have to join a gym. Other suggestions by Hoffman (2010) are:

- Take the stairs instead of the elevator;
- Buy a pedometer (step counter) and increase your number of steps daily;
- Take frequent breaks throughout the day to stand, stretch, and take short walks; and
- Check the pantry. Lift cans, detergent bottles, or anything heavy will build muscle. The patient may do 3 sets of 10 lifts with each hand with any can or bottle that is heavy (that they can handle of course).

Don't ever leave them alone to exercise or walk, even if you are only a person that they talk with during this "exercise bout". The reasons for this are potential seizures, balance problems and even muscle weakness that these patients may experience. This will make them feel at ease in most cases and will not feel like exercise (Jefford *et al.*, 2008).

2.15.3 Type and duration of exercise intervention prescriptions

How much exercise the patient does, depends on how fit the patient is generally. A brain tumor patient's usually are measured according to the Karnofsky Performance Scale (See Table 2.7). This scale will help to provide the Exercise Professional working with the patient's level of physical functioning.

Any patient above the >60, may exercise to a certain extent that is prescribed by the Exercise specialist/Biokineticist. Being at a low level if the patient is at 60, the patient must start slowly and if the patient did not exercise in the past, he or she must build up a level to a recommended fitness level. According to Courneya (2010), the key factor is to start slowly and build your body's energy over time. The patient's body is going through a lot of changes and "hammering" and it is necessary to challenge it gradually (Hoffman, 2010). The patient that is building up to a recommendable exercise level must be advised not to do too much one day, because they will "pay" for it the next day. They also need to know that they do not have to train more than yesterday, because some days the patient might have more energy than other days (Cancer Research UK, 2009).

The National Guidelines recommend 30 minutes of moderate activity 5 or more days a week for cancer patients. The American College of Sports Medicine notes that for weight management and improved muscle strength, resistance training carried out 3 days per week is optimal. As for an "ordinary" cancer patient, the brain tumor patients also needs to do stretching before and after any exercise is critical for increasing flexibility and prevention of injury (Ingram & Visovsky, 2007). According to Velthuis *et al.* (2009) they found that the general exercise prescription for people undertaking or having completed cancer treatment is low to moderate intensity, regular frequency (three to five times per week) for at least 20 minutes per session, involving aerobic, resistance or mixed exercise types.

It is important to notice that the physical components goals includes maximizing range of motion, increasing or sustaining flexibility, enhancing endurance through gradually increased intensity of strengthening and conditioning exercises (Brown *et al.*, 2006). According to the Cancer Research Institute, UK (2009) weight bearing exercises (running, rowing – any exercises where your bones are doing some work) may also protect in thinning of the bones or preventing decreasing in bone density or osteoporosis.

The following components need to be included into the exercise intervention protocol for the best possible results for the brain tumor patient's health:

1. Flexibility is one of the exercises that is emphasized in the exercise protocol program, because it relieves joint stiffness and pain and at some time, improve overall mobility and range of motion.

Other benefits of stretching include according to Hoffman (2010):

- Enhance performance of ADL;
 - Improvement of mobility and independence;
 - Improvement and maintenance of posture and muscle balance; and
 - Promotion of physical and mental relaxation.
2. Aerobic exercises such as brisk walking, jogging and swimming are the kind of exercises that burns calories and helps lose weight. Aerobic exercise also builds cardiovascular fitness, which lowers the risk of heart attack, stroke and diabetes (Hoffman, 2010). For brain tumor patients, these types of exercises must be done at a moderate fashion. For example, swimming may include just walking in the swimming pool or do some kind of aerobics with a pool noodle.
 3. Resistance training that will be with light weights with more repetitions in a set will build muscle strength. Many cancer patients loose muscle mass and gain fat mass during cancer treatment (Hoffman, 2010).

These three components above that will be in the prescribed program, will focus on just sustaining daily living capacity and the quality of how tasks are done in and around the patient's home or living environment. The purpose for this is that the patient will only be helping themselves through these exercises as well as better their ADL environment. Therefore they will know there limits around their home and can only work on that. So this means that the patient's home-based or clinic-based exercises will be individualized by the Exercise Specialist/Biokineticist, because the professional will notice the patient's

immediate need of what component in the exercise program needs the most attention or first attention.

2.15.4 Cardiovascular component of exercise intervention

Endurance exercises are usually the component used in targeting the cardiovascular system including the heart muscle and the lungs or in other words the “oxygen delivery system”. The effect of long-term endurance exercise intervention can be seen both in the resting state and during physical activity. In general, the heart muscle and associated vascular structure become stronger, improving the capacity to accept and deliver blood. In this case the prescription of aerobic exercise in the patients program, will help improving the resting heart rate of the patient and will therefore make the heart stronger (Schneider *et al.*, 2003).

By strengthening the patient’s cardiovascular system, the patient will have lung function capacity that mean less or no breathing problems; the heart muscle will become stronger and therefore pump more the oxygenated blood more efficiently to various part of the body and will optimize the function of the body. The stronger the heart muscle the larger the stroke volume which means the heart does not have to beat as often to produce the necessary cardiac output. Aerobic exercises also lead to a slight lowering in the diastolic and systolic blood pressure and an increase blood volume and production of red blood cells, with concomitant of hemoglobin concentration (Schneider *et al.*, 2003).

A study done by Schwartz *et al.* (2006) in McNeely *et al.*, 2006 on cancer patients’ bone density of the lumbar spine using dual x-ray absorptiometry and reported that subjects participated in weight-bearing aerobic exercises had significantly less bone density loss than patient that did not do weight-bearing exercises. In this type of programs endurance exercise just focus on the aerobic system and not working against very high loads like weight training that initiate muscle strengthening, but more weight-bearing exercises. If we look at what influence the aerobic type of exercise has on the cancer patient it is a well research conclusion that were reached, because it gives the patient a

higher stroke volume of the heart, greater cardiac output, increased blood volume, and increased hemoglobin concentration, greater lung volume, increased diffusion capacity at rest and during exercise. It also prevents loss in muscle mass, bone density, decrease body fat and improve other health related problems like cholesterol or high blood pressure. All of which will improve the patient's functional capacity, making daily tasks more manageable (Schneider *et al.*, 2003; McNeely *et al.*, 2006).

2.15.5 Intensity of exercise intervention

The Borg Rating of Perceived Exertion (RPE) of Borg-scale helps therapist of even the patients, when they learn to use it, to determine the intensity of exercise they can tolerate. The scale ranges from 6 (no exertion) to 20 (maximal exertion) (Cancer Treatment Centers of America, 2008). The Borg scale measures exercise as any activity that increases heart rate. The exercise program of a brain tumor patient is usually not strenuous, so in most cases the patient will exercise at a lower level of normal exertion, at more or less 45-55% of their maximal heart rate, according to my best knowledge through the literature and experience. The normal individual will achieve 65-75% of their maximal heart rate (Cancer Treatment Centers of America, 2008). All just need to remember that all patients are individualized to the level of their current fitness level as well as the stage of cancer diagnosis.

For a brain tumor patient, exercise will pertain at a lower intensity and the patient will still reap the benefits of the positive influence that exercise have on the human body. Physical fitness cannot only increased at lower levels of exercise intensity, but evidence that psychosocial factors such as self-efficacy or self-esteem can be high in adults that do not have high levels of cardiorespiratory functioning, as indicated by resting heart rate levels (Wiggins, 2004).

2.15.6 Exercise termination

After an exercise program has been set for the patient by their health care professional, the patient will be informed how and when to the exercises. Due to its home-based protocol in most cases, the caregiver will always be present when the patient is

exercising. Like any other chronic or life-threatening illnesses, there are always some symptoms to look out for when NOT to exercise or when to pass when they exercise.

According to Jefford *et al.* (2008) they have to set the following criteria for when not to continue or terminate exercising and see their oncologist or specialist before proceeding with their exercise program:

- Light-headedness or dizziness;
- Excessive shortness of breath;
- Chest pain;
- Excessive tiredness; and
- Persistent joint or muscle pain.

According to Courneya (2010), CRF may also lead to exercise termination, but only for a short time. The patient must rest a while and then start slowly again and build up. We must also remember that any cancer patient is not too different from the general population, because musculoskeletal injuries do occur in that population as well. Soreness, strains and sprains are the most common injuries that may terminate their exercises for a while (Hoffman, 2010). It is then important to get help from a Physiotherapist for passive exercise strengthening or mobilization and get back to the exercise program as soon as possible.

2.16 HOLISTIC APPROACH IN EXERCISE PRESCRIPTION FOR THE BRAIN TUMOR PATIENT

Cancer survivors are often highly motivated to seek information about food choices, physical activity, and dietary supplement use to improve their treatment outcomes, quality of life, and survival (Doyle *et al.*, 2008). When a person is diagnosed with any type of cancer, it is important to maintain optimal fitness, namely physically, nutritional fitness, emotional fitness, immunological fitness. These aspects are fundamental to fighting a disease no matter what.

As Biokineticist or Exercise Specialists, we have a holistic approach to the patient and this involves the aspects of the emotional-, spiritual-, physical- and social aspects. This means that all aspects of the person will be taken into account when setting the treatment approach.

1. The *emotional component* sought to address the psychological distress and therefore emphasizing the cognitive-behavioral approach. Strategies like communication, prioritization, assertiveness and stress-management for instance. Each exercise session can end with a relaxation exercise that includes progressive relaxation, guided imagery and deep breathing (Brown *et al.*, 2006).
2. *Spiritual component* addresses the spiritual concerns of those facing this life threatening disease (Brown *et al.*, 2006). Individualized sessions may be set for each patient after or before sessions to discuss frequent topics like grief, guilt, hope, meaning and purpose of all aspects that goes with this illness. Religious beliefs, death and help people believe in the afterlife and that this is not totally the end, but the beginning.
3. *Social components* identify the area of need and ways to improve social support. In exercise sessions, if it is clinic-based or home-based, the patient will interact either with other cancer patients or with his or her spouse/caregiver. These people tend to encourage each other and built a social network that will in most cases help with most of the holistic approach that I strive for in this study. According to Gillison *et al.* (2009) found that an individual's most important determinants for social QoL may continue to be their close friends or family, leaving the group exercise settings to be transmitted through self-efficacy and enjoyment, as suggested by the improvements found in the psychological domain. Prior investigation has shown that group intervention has a better outcome as they promote adherence, and thereby provide better exercise exposure.

2.17 FACTORS FOR CONCERNS SURROUNDING EXERCISE INTERVENTION

McTiernan identified factors that influence physical activity adoption in cancer survivors such as reduced cardiac reserves or other cardiac conditions related to treatment, deconditioning and loss of muscle mass, neuropathies, increased intracranial pressure, increased risk of infection, lymphedema, pain, amputations and bone metastases (Ingram & Visovsky, 2007).

Depending on the patient's stage of tumor diagnosis, it will usually give us the way how they will adapt to the exercise intervention. Some patients may be able to begin and sustain a level of exercise intervention that has been prescribed to them and others will either deteriorate or rather be slower in their exercise bouts. It is important to remember that a primary brain tumor patient will deteriorate closer to the end, due to the growth in the brain. The main focus and goal of these exercises is to sustain their own quality of life for as long as possible.

According to the study by Ingram and Visovsky (2007) they focus on the idea that the majority of research focused on aspect of CRF and physical function. The believe in most cancer arenas nowadays are the fact to try encourage patients to follow some kind of social, physiological and emotional protocol during this treatment. Therefore the patient may experience some relieve from CRF or other factors that may impact on their ADL. In this time of uncertainty they will need to focus on their ADL in order to help improve or sustain their QoL.

2.18 PRIMARY BRAIN TUMOR AND CARE OF THE PATIENT

A very successful study by Scoccianti *et al.* (2010) in Italy done over the period from 2002 and 2007 were the largest survey of GBM patients over a very short time of observation. It showed that the treatment of this tumor has changed significantly. So despite the different centers and patients that were used in this study, showed a different management for each center and each patient, obviously, there were still a few protocol types of medicine used in all centers to care for each of these patients. Thus, their analysis reflected an important period of change in the multidisciplinary

management of GBM or any primary brain tumor for that matter. The multidisciplinary team will focus on bettering the quality of life of the brain tumor patients. This could incorporate management of those symptoms that are reversible and those that dramatically impact on people's lives such as fatigue and neuro-cognitive difficulties, and tailored rehabilitation programmes that involve regular reassessment of symptoms and continuity of care (Molassiotis *et al.*, 2010). The survival rate for GBM has increased slightly the last few years, but significantly improved with a small but noteworthy number of relatively long-term survivors (Scoccianti *et al.*, 2010).

These types of studies to improve the quality of life of the brain tumor patients will give patients and their families some new hope of accepting the challenges of this disease. In the study done by Brown *et al.* (2006) they aimed to involve the caregivers to sustain contact in their new studies when they investigate different aspects of cancer patients including brain tumor patients, this will help improve and sustain the intervention beyond just the active treatment period. Despite of the new findings of treating the disease of a brain tumor, the patient and their families still need to be mentally prepared for all the emotional pain and despair that they will experience throughout this process of treatment by the oncologist and other members of the multidisciplinary team.

2.18.1 The brain tumor patient and management with the prognosis

The idea of cancer is that the person is diagnosed and after a certain time frame, this person will die due to the illness or complications or treatment of it. Cancer is seen as a chronic disease and the term "survivorship" does not span from remission till death, but from day of diagnosis till the day of death. So this means remaining a survivor of this disease until the moment of death (Seyama *et al.*, 2010). So "living in the moment", as oppose to "long-term survival"- is an important concept that can form the base of treatment of these type of patients.

Cell growth in brain tumors are extremely fast and the median survival rate of patients with Glioblastoma Multiforme is 9 to 12 months with a 5-year survival of 2% (Seyama *et al.*, 2010). According to this statistic, brain tumors do not have a very good prognosis at

this stage of time, and it means that the patient and his/her family must adapt to the new situation of illness due to this tumor very quickly. These changes have a huge impact on a family and it affects the daily way of living.

A lot of impairments due to the brain tumor may occur during patient's illness. Impairments like movement and communicative skills may cause that the patient feel helpless and hopeless. The family on the other hand must adapt to the new lifestyle of helping and adjusting to the patient's way of living. Support is a very important part of the treatment protocol for every brain tumor patient. It provide the patient with support to cope and adjust with their life limitations that are not amenable to immediate change (i.e. inability to drive) and work with patients to identify alternative options that are acceptable and feasible to them (Molassiotis *et al.*, 2010). Both parties may experience despair and anxiety during the time of treatment and the anticipation of death of the ill family member make the feel depressed and sometimes make them go in to a state of mourning (Seyama *et al.*, 2010). With this state of mourning, stress can become a problematic factor for that patient's household and it is necessary to find some kind of stress management activities to help the household cope with all the changes regarding the family member's illness.

2.18.1.1 The caregiver, the patient and QoL

Quality of life is an important area of clinical neuro-oncology that is increasingly relevant as survivorship increases and as patients experience potential morbidities associated with new therapies (Liu *et al.*, 2008). In review done by Bampoe *et al.* (1998) they examined several aspects and problems associated with the past, present, and future applications of quality of life assessments in neuro-oncology. Quality of life will have a tremendous impact on the patient as well as on the caregiver or the people closely related to the patient. Due to the fact that mortality and morbidity of low-grade and high-grade brain tumors differ, it is sometimes impossible to establish the best way to approach the patient and their families with regards the prognosis. The prognosis will usually have an impact on the patient's way of looking at the diagnosis and it will definitely influence their psychological well-being and thereafter the QoL. To date,

reports on QoL have been primarily qualitative and focused on specific symptoms such as fatigue, sleep disorders, and cognitive dysfunction (Liu *et al.*, 2008). Researchers noticed the inadequacy of the almost exclusive use of physical functioning assessments, response to cancer therapy, and the patients' survival time as endpoints when evaluating therapeutic regimens are becoming increasingly apparent (Bampoe *et al.*, 1998). In the case of brain tumor patients, different treatment regimens and prognosis needs to be taken into consideration due to the numerous situations, symptoms and other problems that may occur or develop during from the time of diagnosis. All of these factors will have an influence on the patients QoL outcome. The QoL will include functioning-, emotional-, psychosocial-, social- and cognitive well-being.

There are increasing evidence that the mind (cognitive behavior) does indeed matter in the fight against cancer and that preserving psychosocial functioning, and instituting therapeutic measures that improve it, positively influence survival and QoL (Bampoe *et al.*, 1998). The influence of the social world like family, friends etc. will have therefore an impact on the patients overall well-being.

The main person that is "responsible" for the brain tumor patient's well-being during this time of illness is called the caregiver. The caregiver could be in the form of a spouse, any close loved one that stays with the patient (like children or close friends) or it could be a nurse from a Hospice center. It is important the caregiver is capable to handle the patient in all the facets of the treatment, and therefore it is necessary that the caregiver is informed of all the aspects of the disease.

Caregiver training can be very appropriate to incorporate in the multidisciplinary team; because it can help the caregiver to help the patient adapt to all the changes especially impairments of the body (Molassiotis *et al.*, 2010), as well as to cope and adapt to the change in the household.

The changes have a huge impact on the patient and the patient's family and can be very stressful on all of their daily routines and their QoL. In a study from Janda *et al.* (2007) they found that, on average, patients with a brain tumor and their carers live with a

clinically significant reduction in their overall QoL as compared to the general population. It was also found that preoperatively, QoL has been reported to be worse in patients with highly malignant tumors and those with tumors located in the right hemisphere or the anterior cortex as compared with patients with tumors located in the left hemisphere or the posterior cortex (Janda *et al.*, 2007). According to these findings, it is important that the caregiver of the specific patient's diagnosis have all the information. With this information they can be "trained" to understand what is been expected of them and how to handle the symptoms of the patient and situation accordingly.

A model (Figure 2.2) for future QoL research has been established by Liu *et al.* (2008). This model is to help understand all the different aspects that contribute to the deterioration of the primary brain tumor patient's quality of life. There are *tumor factors*, *patient factors* and *treatment factors*.

- Tumor factors include the tumor laterality, size and location,
- Patient factors include demographic characteristics and comorbidities that may affect perceptions and symptom experience, and
- Treatment factors include surgery, chemotherapy, radiotherapy, and medication that can cause or relieve symptoms (Liu *et al.*, 2008).

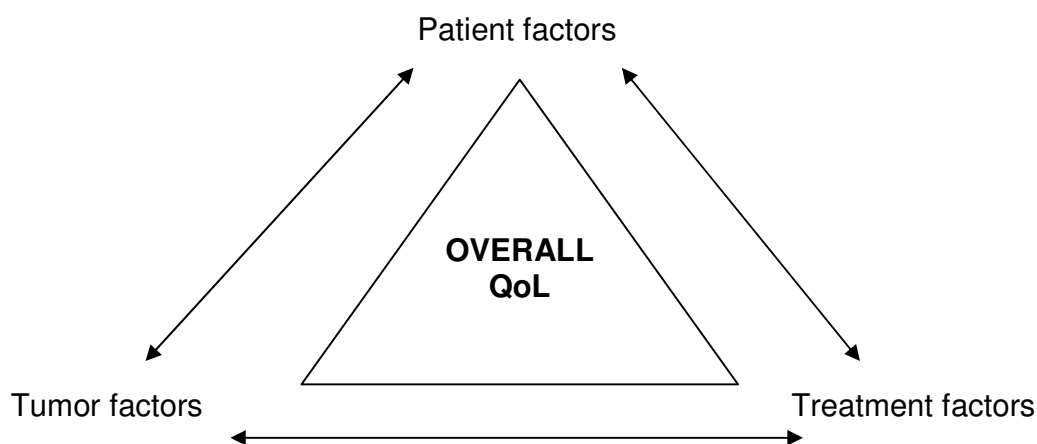


Figure 2.2 : Model to evaluate effects of different factors on brain tumor patients' overall quality of life (QoL) (Liu *et al.*, 2008).

2.18.1.2 The caregiver, patient and ADL

It is important to acknowledge that the caregiver has a huge influence on the patient's well-being, QoL and the way in which the patient's approach each day. It is very important, as hard as it may sound, the caregiver be a positive influence to the patient. As we already know, fatigue is one of the main problematic symptoms that any cancer patient experience during his or her treatment. If the caregiver and the patient know when the fatigue is at its worst, like after radiotherapy for argument sake, they can plan their daily activities around this. By becoming aware of the personal energy patterns of the patient, they can learn to conserve energy and develop ways to use their limited amount of energy efficiently (Armstrong *et al.*, 2004). The caregiver is basically running the patient's as well as his or her own life, which could become very exhausting.

During the intervention study by Janda *et al.* (2007) they found during the group discussions and qualitative interviews, those carers of patients with a brain tumor reported that caring has a significant impact on their own well-being and ADL. This reflected in the significant correlation between patients' and carers' overall quality of life in the same study, with patients and carers in the same household reporting similar reductions in especially in emotional well-being and social well-being. Similar associations have been made in studies done in breast- and colorectal cancer samples, indicating that supportive care need to be directed to the patients as well as their carers to effectively alleviate distress (Janda *et al.*, 2007). With most measurement like with anxiety, mood, stress and depression the patients and carers showed high correlation.

I already explained through the above literature study the positive influence exercise have on the human brain, as well as on the human body it is just "common sense" to initiating physical exercise as an intervention with all cancer patients through all these proven statements. The important thing though, is to remember that the type of exercise program will differ from patient to patient and from one type of cancer to another.

There are considerable and growing evidence that physical activity and/or exercise behavior plays a role in the patient's perception of his or her quality of life (Gillison *et al.*, 2009).

The function that exercise should play, according to what I want to investigate in this study is, is that the person can keep their quality of life for longer and it is not a cure or a way to lengthen the patient's life.

QoL is important in any person's life in terms of doing daily personal tasks by themselves and due to the fact that they want to be and feel independent from other people as long as possible. To be dependent on somebody of common daily tasks is great frustration for most people, no matter what type of illness they may have. The main aspect is then organization. Organization of daily task according to the patient's fatigue levels or treatment times, organizing the home i.e. household implements to better the going around the house by themselves for example, railings in the corridor to hold on to when walking, grab railings in the bathroom or toilet to help them up or extension bars to assist the patient instead of asking for assistance. This is also a way to manage fatigue (Armstrong *et al.*, 2004).

The approach of making the daily living for the patient easier by altering some aspects in the home environment will help them experience their illness differently, as well as improving their view of the QoL that they are experiencing.

The study done by Scoccianti *et al.* (2010) and colleagues provided a benchmark analysis of current patterns of clinical practice and outcomes for patients with GBM. It revealed major changes in GBM patient care, highlighted the greater diagnostic and therapeutic resources that are now availability to GBM or higher-grade glioma patients.

2.18.1.3 The caregiver, the patient and exercise

When a primary brain tumor patient is put on a program of exercise intervention, it is important to realize that this type of patient needs constant help and assistance during this treatment.

Through various literature studies, we know that a brain tumor patient may have certain symptoms that they may have balance-, depth perception problems and may have episodes of grand mal seizures that could place this patient in grave danger of hurting themselves in the process of exercise intervention. The caregiver can also only be the patients “right hand” in the case of support, like noted before, someone who they can talk to when they exercise.

2.19 RESEARCH ON MANAGEMENT PROGRAMS FOR BRAIN TUMOR PATIENT AND FAMILIES

A study done by Seyama *et al.* (2010) where 12 families were observed, they conducted a longitudinal study using semi structured interviews, which they analyzed with the Modified Grounded Theory approach. The purpose for their study was to research how families of patients with Glioblastoma, or for that matter any brain tumor, come through emotional pain and prepare for the patient’s parting with them. They wanted to prepare a structured plan or program to support the families with their sick loved ones. Another study done also had the main aim of promoting clinical research on the management of brain tumors and to develop educational programs for improving the case of neuro-oncological patients. They found that there is emotional pain, by the family and the patient that will never go away, that started with the diagnosis (Scoccianti *et al.*, 2010). This pain will remain until death for the patient and it will carry on with the family until they reconcile the polar emotional states of hope and pain (Scoccianti *et al.*, 2010). In terms of nursing support, according to this article by Seyama *et al.* (2010), their results suggested the need to adjust two factors mentioned namely “one’s own reconciliation with pain” and “factors that increase emotional pain”, while trusting in the strength of involved families, and intervening from an empowerment perspective, to achieve problem resolution (Seyama *et al.*, 2010).

A very successful study done by Scoccianti *et al.* (2010) in Italy over the period from 2002 and 2007, where they've done the largest survey of GBM patients for a very short time of observation, showed that the treatment of this tumor has changed significantly. So despite the different centers and patients that were used in this study, showed a different management for each center and each patient obviously, there were still a few protocol types of medicine used in all centers to care for each of these patients. Thus, their analysis reflected an important period of change in the multidisciplinary management of GBM. The survival rate for GBM has increased slightly, but significantly improved with a small but noteworthy number of relatively long-term survivors.

This means that there will definitely be a place for exercise intervention in this multidisciplinary environment.

CHAPTER 3

METHODOLOGY

3.1 OBJECTIVES

- The Objective of the study was to investigate the exercise behavior, preferences and perceptions of Quality of Life of Primary Brain Tumor Patients.

In order to reach the objective above the analysis of results had the following aims:

- To determine patients' perceptions of the Physical, Social, Emotional and Functional well-being as well as their perceptions of fatigue experienced and their quality of life;
- To look at the relationship between Physical, Social, Emotional, and Functional well-being and perceptions of Fatigue and Quality of Life;
- To determine whether statistically significant differences existed on between those who did exercise and those who didn't in terms of reported Physical, Social, Emotional, and Functional well-being and perceptions of Fatigue and Quality of Life;
- To determine whether they participated in exercise before diagnosis, during treatment and after treatment;
- To determine patients' exercise preferences;
- To determine patient's beliefs regarding exercise; and
- To determine their intentions to exercise in the following months and through which media they would like to receive information regarding exercise programs.

3.2 METHODOLOGY

The sample consisted of 14 brain cancer patients in various stages of the illness. A purposeful sampling method was used to collect the data. The research design was done by making use of a survey with patients who were diagnosed and willing to participate in this survey. An Exercise and Quality of Life questionnaire (Fact-Br) was compiled that focused on the areas identified in the objectives of this study. The Fact-Br

scale contains a variety of measuring areas that are linked to the quality of life and experience of brain tumor patients. It contains 53 questions with high validity and good psychometric properties and efficacy to assess QoL in patients in the population (Preedy & Watson, 2010).

3.3 STATISTICAL ANALYSIS

The collected measurements were captured on a computer and analyzed by means of the SPSS package (Statistical Product and Service Solutions). The following statistical techniques were used to do the analysis.

3.3.1 Descriptive statistics

“Descriptive statistics is a medium for describing data in manageable forms” (Babbie, 1992 : 430). Use was made of Frequency analysis to describe the sample and also to give an indication of trends in the manner in which patients responded to the various questions in the questionnaire. Descriptive statistics was used to give an indication of patients’ scores on the calculated indexes of Physical, Social, Emotional, and Functional Well-being and perceptions of Fatigue and Quality of Life. These descriptive statistics included the number of participants, minimum and maximum values, mean scores and standard deviations.

Mean score: The mean score is used to describe *central tendency*. The mean score is computed by adding up all the applicable values and dividing it by the number of cases. (Trochim, 2010). The mean scores of indexes were calculated for those who participated in exercise versus those who didn’t, for the purpose of comparison.

3.3.2 Inferential statistics

“Inferential statistics assists you in drawing conclusions from you observations; typically, that involves drawing conclusions about a population from the study of a sample drawn from it” (Babbie, 1992). Since the sample was relatively small and consisted of only 14 patients, use was made of non-parametric statistics to analyze the data. The recruitment of primary brain tumors patients are fairly difficult due to the patients’ time of diagnosis

and the time of survivorship that is very limited. Non-parametric tests, also known as distribution-free tests, are a class of tests that does not rely on a parameter estimation and/or distribution assumptions (Howell, 1992). The major advantage attributed to these tests is that they do not rely on any seriously restrictive assumptions concerning the shape of the sampled populations and thus accommodates small samples as in the case of this study. The inferential statistics were firstly used to determine whether there were any relationships between the concepts tested by the indexes. Secondly, it was used to determine whether statistically significant differences existed between patients who did participate in exercise versus those who didn't, on each of the indexes.

- I. **Spearman rank-order correlations:** Spearman's rho was used to determine the correlations between Physical, Social, Emotional, and Functional Well-being and perceptions of Fatigue and Quality of Life. Spearman's rho is a non-parametric version of the Pearson correlation coefficient, based on the ranks of the data rather than the actual values. It is appropriate for ordinal data, or for interval data that do not satisfy the normality assumption. Values of the coefficient range from -1 to +1. The sign of the coefficient indicates the direction of the relationship, and its absolute value indicates the strength, with larger absolute values indicating stronger relationships (SPSS Manual) (Howell, 1992).

- II. **The Mann-Whitney Test:** The Mann-Whitney test is used for testing differences between means when there are two conditions and different subjects have been used in each condition. This test is a distribution-free alternative to the independent samples t-test. Like the t-test, Mann-Whitney tests the null hypothesis that two independent samples (groups) come from the same population (not just populations with the same mean). Rather than being based on parameters of a normal distribution like mean and variance, Mann-Whitney statistics are based on ranks. The Mann-Whitney statistic is obtained by counting the number of times an observation from the group with the smaller sample size precedes an observation from the larger group. It is especially sensitive to population differences in central tendency (Howell, 1992). The

rejection of the null hypothesis is generally interpreted to mean that the two distributions had different central tendencies, in other words, that there is a significant difference between the two groups on a specific variable measured. This test was used to determine significant differences between those patients who did participate in exercise versus those who didn't participate, on each of the indexes calculated.

CHAPTER 4

RESULTS AND DISCUSSION

4.1 RESULTS

The results of this study will be presented in the following order.

- Description of the sample;
- Results of the analysis of indexes: Physical, Social, Emotional, Functional Well-being, Fatigue and Quality of Life;
- Results of the analysis of patients' participation in sport, exercise preferences;
- Results of the analysis of patients' beliefs regarding exercise and their intentions to exercise in the coming months; and
- Patient preferences regarding the media through which they would like to receive information regarding exercise programs.

All the analyses are presented in technical addendums Appendix A and B for references purposes.

4.2 DESCRIPTION OF THE SAMPLE

The following section will give a description of the sample in terms of their demographical information, in other words the everyday lives of these patients, including their education, employment status, marital status, exercise behavior, exercise preference etc. As mentioned previously, the sample consisted of 14 patients who have been diagnosed with higher grade primary brain cancer.

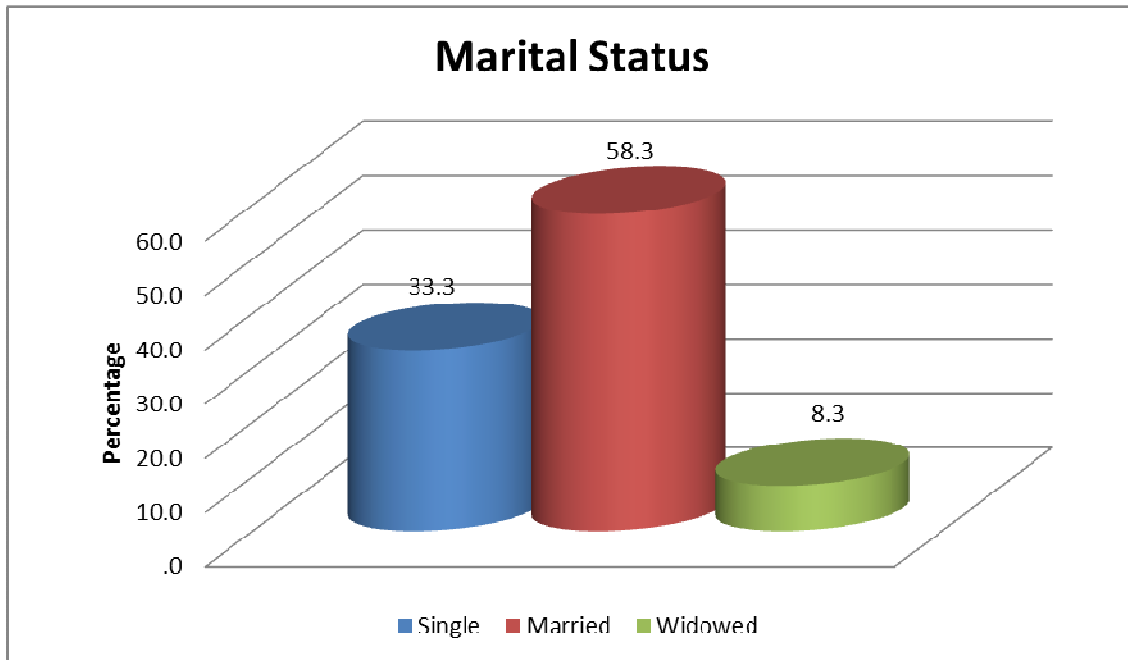


Figure 4.1: Marital status of questionnaire participants

More than half of the patients were married (58.3%), with a third (33.3%) being single and 8.3% was widowed.

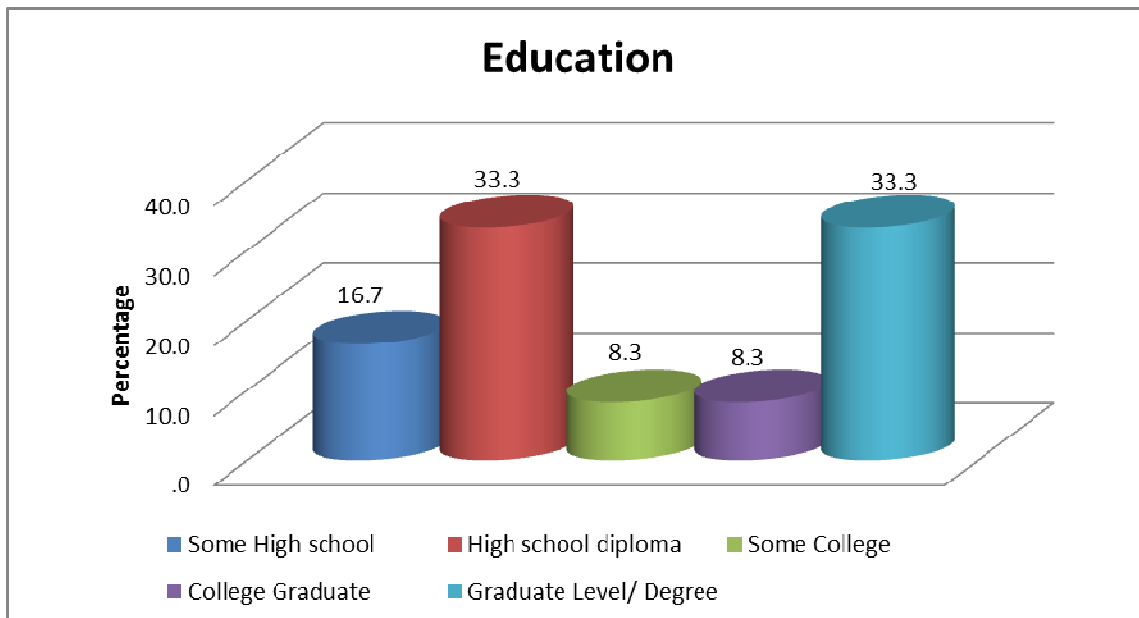


Figure 4.2 : Education of questionnaire participants

A third of the patients had high school diplomas, with another third (33.3%) indicating that they had a graduate level qualification or degree.

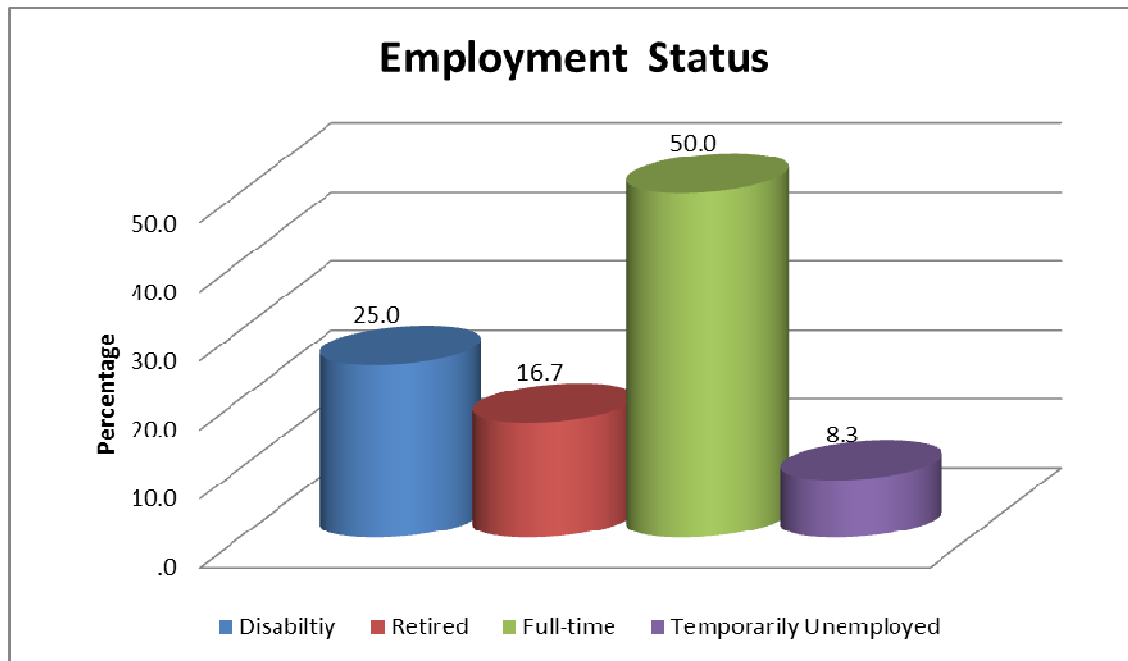


Figure 4.3 : Employment status of questionnaire participants

Half of the patients (50%) were full-time employed with a quarter (25%) indicating that they were disabled. Sixteen point seven percent (16.7%) were retired with 8.3% temporarily unemployed.

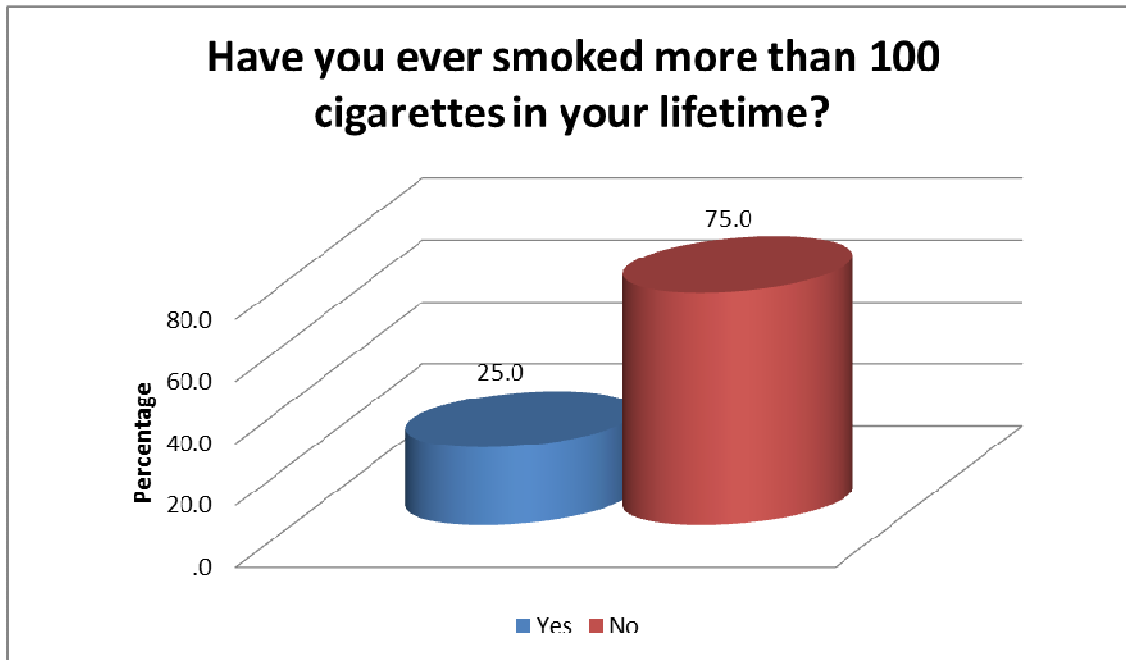


Figure 4.4 : Cigarette smoking habits of participants

Two thirds (75%) of the patients indicated that they have smoked more than 100 cigarettes in their lifetime according to the above figure.

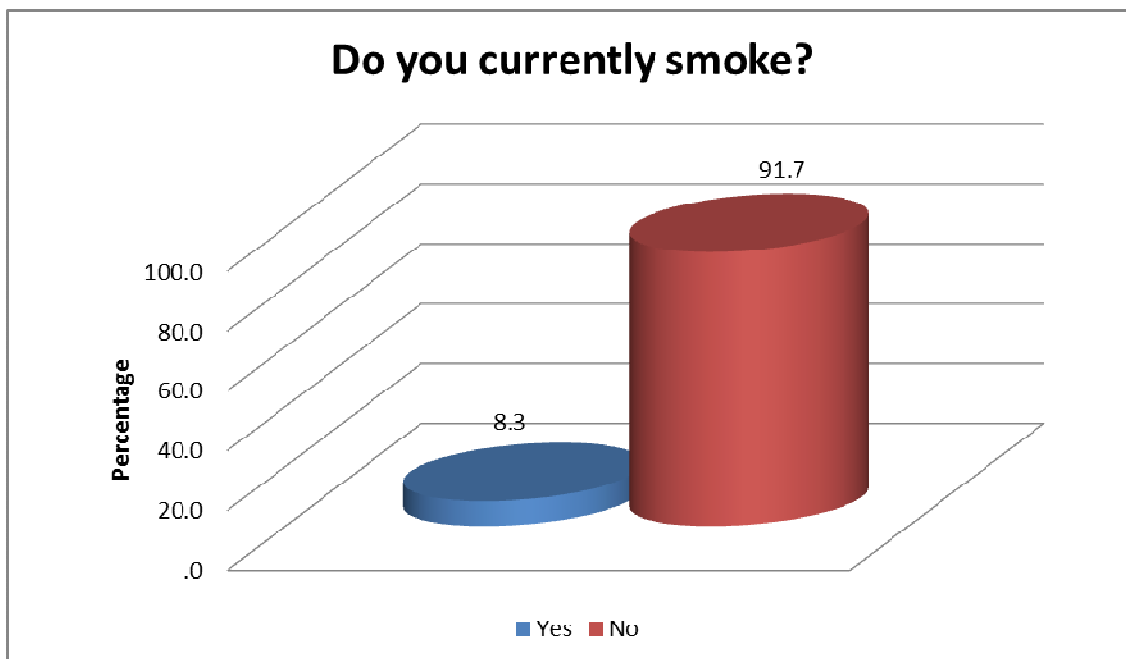


Figure 4.5 : Current smoking habits of participants

The majority of patients (91.7%) did not smoke at the time of the survey. This shows us a decline in cigarette smoke from time of diagnosis to time of the survey.

4.3.1 Results of the analysis of indexes: Physical, social, emotional, functional well-being, fatigue and quality of life

The results of patient's responses to the questions relating to Physical, Social, Emotional, Functional Well-being, Fatigue and Quality of Life are presented in Tables 4.1 to 4.7. Positive trends will be coloured in *green* with more negative trends coloured *orange*. The second part of this section will take a look at the correlations between the indexes as well as whether statistically significant differences could be detected between those patients who did participate in exercise versus those who didn't.

4.3.2 Results of patients' responses to the questions pertaining to the indexes of physical, social, emotional and functional well-being, fatigue and quality of life

Table 4.1 : Results of responses on questions pertaining to physical well-being

| PHYSICAL WELL-BEING | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|---------------|------------|--------------|----------|-------------|-----------|
| I have a lack of Energy | Valid Percent | 7.1 | 35.7 | 21.4 | 14.3 | 21.4 |
| I have nausea | Valid Percent | 57.1 | 21.4 | 14.3 | 7.1 | |
| Because of my physical condition, I have trouble meeting the needs of my family | Valid Percent | 35.7 | 28.6 | 7.1 | 14.3 | 14.3 |
| I have pain | Valid Percent | 57.1 | 21.4 | 7.1 | 7.1 | 7.1 |
| I am bothered by side effects of treatment | Valid Percent | 14.3 | 35.7 | 7.1 | 21.4 | 21.4 |
| I feel sick | Valid Percent | 57.1 | 14.3 | 14.3 | 7.1 | 7.1 |
| I am forced to spend time in bed | Valid Percent | 57.1 | 28.6 | 7.1 | .0 | 7.1 |

The results in Table 4.1, indicated that in most cases the patients indicated that they do not suffer, or suffer very little from the symptoms of the illness. Aspects experienced more often by patients was a lack of energy and being bothered by the side effects of the treatment. Almost a third (28.6%) also indicated that because of their physical condition, they had trouble meeting the needs of their families. Due to these problems that the patient experiences in this regard the patient will need extensive help from his/her family or caregiver. Studies has investigated the specific challenges that family caregivers face when caring for patients experiencing significant neurocognitive and neurobehavioral disorders associated with brain tumors (Schubart *et al.*, 2008). This study found that the family caregivers provided extraordinary uncompensated care involving significant amount of time and energy and requiring the performance of tasks that are often physically, emotionally, socially or financially demanding (Schubart *et al.*, 2008). The challenges will change according to the development and escalating of the disease.

According to Table 4.2, it shows a positive side to the cognitive- and emotional well-being of the patients that completed the survey. Although the overall responses were in the median, which indicate that the patients are not totally comfortable that what they experience, but are still positive in most of the cases. The way of positive thinking in this situation is of cardinal value, but due to this disease, it is not always possible. Functioning of the brain in terms of attention, memory and executive functioning will become impaired during the course of the disease or treatment. Although these impairments are not severe in nature, in general, but they can have a huge impact on the patients' daily lives. Subjective cognitive symptoms are among the most common neurologic problems reported by brain tumor patients (Gehring *et al.*, 2008). The cognitive deficits that these patients experience will most definitely influence the emotional well-being of the patients.

Table 4.2 : Results of responses on questions pertaining to social/family well-being

| SOCIAL/FAMILY WELL-BEING | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|--|---------------|-------------------|---------------------|-----------------|--------------------|------------------|
| I feel close to my friends | Valid Percent | | 7.1 | 14.3 | 28.6 | 50.0 |
| I get emotional support from my family | Valid Percent | | 7.1 | | | 92.9 |
| I get support from my friends | Valid Percent | 7.1 | 7.1 | | 7.1 | 85.7 |
| My family has accepted my illness | Valid Percent | | | 14.3 | 7.1 | 78.6 |
| I am satisfied with family communication about my illness | Valid Percent | | | 14.3 | | 85.7 |
| I feel close to my partner (or the person who is my main support) | Valid Percent | | | | 21.4 | 78.6 |
| I am satisfied with my sex life | Valid Percent | 9.1 | 27.3 | 9.1 | 9.1 | 45.5 |

The majority of patients indicated that they did get support from family and friends and that their illness was accepted and they experienced communication about their condition positively. Slightly fewer patients (50% and 45.5% respectively) indicated that they felt close to their friends and were satisfied with their sex lives (see Table 4.2). As mentioned on the previous page, positive attitude, family and/or caregivers are very important to help fulfill the everyday needs of a brain cancer patient. The needs of the brain cancer patient will change throughout the development of the disease. Lehmann et al. identified needs of the cancer population and in their study it showed that 438 of 805 patients had impairments and/or functional limitations (Gerber, 2001). This means that the dependence level will become higher. The dependence is due to psychological distress, general weakness, ADL's, pain, balance and ambulation, work-related problems etc. (Gerber, 2001).

It is clear that the patients need to have close support and understanding of the people close to them. The "social network" that surrounds them will have an impact on the patient's emotional well-being. In this case, the family and friends need to support the

patient at mostly at an emotional- and social level.

Table 4.3 : Results of responses on questions pertaining to emotional well-being

| EMOTIONAL WELL-BEING | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|--|---------------|------------|--------------|----------|-------------|-----------|
| I feel sad | Valid Percent | 21.4 | 42.9 | 14.3 | | 21.4 |
| I am proud of how I am coping with my illness | Valid Percent | | 7.1 | 7.1 | 28.6 | 57.1 |
| I am losing hope in the fight against my illness | Valid Percent | 78.6 | 7.1 | 14.3 | | |
| I feel nervous | Valid Percent | 21.4 | 42.9 | 21.4 | 14.3 | |
| I worry about dying | Valid Percent | 50.0 | 42.9 | | 7.1 | |
| I worry that my condition will get worse | Valid Percent | 15.4 | 46.2 | 15.4 | 15.4 | 7.7 |

The results in Table 4.3 indicates that there was some ambivalence regarding the feelings of sadness with 42.9% indicated that they feel a little bit sad, with 21.4% indicating that they were feeling very much sad. The majority (85.7%) were proud of how they were coping with their illness with 78.6% indicating that they were not losing hope in the fight against their illness at all. Patients indicated that they did not feel nervous or worried about dying or only felt so to a lesser extent. Almost half (46.2%) said that they worried a little bit that their conditions would get worse.

Coping style of the patient towards this illness is important due to the impact it has on different side-effects that they may experience due to chemotherapy and other cancer treatments. Anxiety, depression, nausea that are cause by chemotherapy may impact there emotional well-being (Lerman *et al.*, 1990). Emotions play a significant role in any patient's well-being. Whelan et al. summarized in their study that the main issues or symptoms that patients experience are fatigue, worry and anxiety, sleep disturbances and pain (Gerber, 2001). All of these symptoms impact on the emotions of the patient and may help with the deterioration of the overall well-being. In the study of Gerber (2001), the patients indicated that they needed more education about their disease,

better social support, and help with ADL.

Patients in this study show a very mature way of handling their illness at a level that compliments their QoL. Although some percentage of the patients is nervous about their progress or prognosis, they still have a positive cognitive- and emotional viewpoint on their life.

Table 4.4 : Results of responses on questions pertaining to functional well-being

| FUNCTIONAL WELL-BEING | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|---------------|-------------------|---------------------|-----------------|--------------------|------------------|
| I am able to work (Include work at home) | Valid Percent | 14.3 | 7.1 | 7.1 | 28.6 | 42.9 |
| My work is fulfilling (include work at home) | Valid Percent | 21.4 | | 7.1 | 28.6 | 42.9 |
| I am able to enjoy life | Valid Percent | 14.3 | | | 42.9 | 42.9 |
| I have accepted my illness | Valid Percent | 7.1 | | | 14.3 | 78.6 |
| I am sleeping well | Valid Percent | 7.1 | | 28.6 | 7.1 | 57.1 |
| I am enjoying the things I usually do for fun | Valid Percent | 14.3 | 14.3 | 7.1 | 28.6 | 35.7 |
| I am content with the quality of my life right now | Valid Percent | 14.3 | 7.1 | 21.4 | 35.7 | 21.4 |

Patients' responses regarding their functional well-being were mostly positive (see Table 4.4). The majority of them indicated that they were able to work and found it fulfilling, that they were able to enjoy life and accepted their illness, that they were sleeping well and enjoyed the things they used to do for fun and lastly that they were content with the quality of life they had at that moment. A fifth (21.4%), however, indicated that they did not find their work fulfilling at all, this also depends on what type of work the patient did before falling ill. This 21.4% of this survey might have had a very high demand work setup, which they cannot handle anymore. This may have a huge emotional, social and cognitive effect on the patient.

Patients' responses regarding their experience of fatigue differed considerably from one

another (see Table 4.5). Half to the majority of patients indicated that they did not feel fatigue, weak, listless or tired or only felt so a little bit. The rest of the patients, however, indicated that they did feel this way. While just more than half of the patients indicated that they did not have trouble starting or finishing things, the rest indicated that this was the case in varying degrees. Just more than a third of the patients indicated that they did not have energy or were not able to do their usual activities or could only do so a little bit, while the rest indicated the opposite. More than half (61.6%) indicated that they did not need to sleep during the day or only did so a little bit. Most indicated that they were not too tired to eat (76.9%), with 76.9% indicating that they did not need help doing their usual activities or only did so a little bit. While approximately half of the patients indicated that they did not feel frustrated by being too tired to do the things they wanted to or that they had to limit their social activities because they were tired, the rest indicated that they did feel this way in varying degrees.

Losing of functional well-being is usually brain cancer patients or overall cancer patients' worst fear. Fear of disability and dependence on others for ADL, and the implication is that they are not receiving treatment for these symptoms and concerns (Gerber, 2001). Therefore it is important to establish a secure network of medical information or –team to help patients cope with these concerns, because this will remain a challenge.

Patients' responses regarding their experience of fatigue differed considerably from one another (see Table 4.5). Half to the majority of patients indicated that they did not feel fatigue, weak, listless or tired or only felt so a little bit. The rest of the patients, however, indicated that they did feel this way. While just more than half of the patients indicated that they did not have trouble starting or finishing things, the rest indicated that this was the case in varying degrees. Just more than a third of the patients indicated that they did not have energy or were not able to do their usual activities or could only do so a little bit, while the rest indicated the opposite. More than half (61.6%) indicated that they did not need to sleep during the day or only did so a little bit. Most indicated that they were not too tired to eat (76.9%), with 76.9% indicating that they did not need help doing their usual activities or only did so a little bit. While approximately half of the patients indicated that they did not feel frustrated by being too tired to do the things

they wanted to or that they had to limit their social activities because they were tired, the rest indicated that they did feel this way in varying degrees. According to Table 4.5, it appears that most of the patients still want to be in control of their daily lives despite of the illness. Although, their circumstances did change due to the tumor, they still have the ability to cope with changes in their daily activities. As it grows worse, they will have to adapt even more and make use of their support systems, which should be in place and then they will be able to cope better with their ever changing circumstances.

Table 4.5 : Results of responses on questions pertaining to fatigue

| FATIGUE | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|---|---------------|-------------------|---------------------|-----------------|--------------------|------------------|
| I feel fatigued | Valid Percent | 16.7 | 33.3 | 25.0 | 8.3 | 16.7 |
| I feel weak all over | Valid Percent | 23.1 | 38.5 | 7.7 | 15.4 | 15.4 |
| I feel listless | Valid Percent | 30.8 | 23.1 | 23.1 | 7.7 | 15.4 |
| I feel tired | Valid Percent | 15.4 | 46.2 | 7.7 | 15.4 | 15.4 |
| I have trouble starting things because I am tired | Valid Percent | 23.1 | 38.5 | 15.4 | 15.4 | 7.7 |
| I have trouble finishing things because I am tired | Valid Percent | 23.1 | 30.8 | 15.4 | 23.1 | 7.7 |
| I have energy | Valid Percent | 7.7 | 30.8 | 15.4 | 38.5 | 7.7 |
| I am able to do my usual activities | Valid Percent | 15.4 | 15.4 | 38.5 | 30.8 | |
| I need to sleep during the day | Valid Percent | 30.8 | 30.8 | 15.4 | 7.7 | 15.4 |
| I am too tired to eat | Valid Percent | 76.9 | 7.7 | | 15.4 | |
| I need help doing my usual activities | Valid Percent | 53.8 | 23.1 | 7.7 | | 15.4 |
| I am frustrated by being too tired to do the things I want to do | Valid Percent | 23.1 | 30.8 | 7.7 | 23.1 | 15.4 |
| I have to limit my social activity because I am tired | Valid Percent | 30.8 | 15.4 | 15.4 | 23.1 | 15.4 |

Fatigue is the one of the fearful aspects of being diagnosed with cancer and is most commonly experienced by these patients. This occurs mostly due to cancer related treatments. Furthermore, fatigue may turn into a long-lasting problem and it may persist even years after the end of therapy.

Fatigue is normal and necessary instrument of physiologic self-regulation, which means, it helps you to realize when to stop with a certain activity (Dimeo, 2001). In cancer patients it is a different story though. The fatigue they experience will inhibit them to even do anything, and this promotes stress and anxiety. In this case, the patients will be advised to lower their activity levels, but still be active. Psychological factors, which include depression and anxiety, may play an important etiologic role in the genesis of cancer fatigue. Nerenz et al. found a strong relationship between tiredness and the emotional distress experienced during cancer treatment (Dimeo, 2001). Here the relationship between emotional-, psychological- and functional well-being of the cancer patient can be seen clearly.

Table 4.6 : Results of responses on questions pertaining to quality of life

| QUALITY OF LIFE | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|--|---------------|------------|--------------|----------|-------------|-----------|
| I am able to concentrate | Valid Percent | 14.3 | 14.3 | 28.6 | 21.4 | 21.4 |
| I have had seizures | Valid Percent | 50.0 | 21.4 | | 21.4 | 7.1 |
| I can remember new things | Valid Percent | 7.1 | 21.4 | 14.3 | 28.6 | 28.6 |
| I get frustrated that I cannot do things I used to | Valid Percent | 14.3 | 28.6 | | 21.4 | 35.7 |
| I am afraid of having a seizure | Valid Percent | 35.7 | 7.1 | 21.4 | 7.1 | 28.6 |
| I have trouble with my vision | Valid Percent | 14.3 | 42.9 | 14.3 | 14.3 | 14.3 |

Table 4.7: Results of responses on questions pertaining to quality of life (cont.)

| QUALITY OF LIFE | | Not at all | A little bit | Somewhat | Quite a bit | Very much |
|--|---------------|------------|--------------|----------|-------------|-----------|
| I feel independent | Valid Percent | 21.4 | 7.1 | 21.4 | 14.3 | 35.7 |
| I have trouble with my hearing | Valid Percent | 64.3 | 21.4 | 14.3 | | |
| I am able to find the right word(s) to say what I mean | Valid Percent | 21.4 | 21.4 | 14.3 | 21.4 | 21.4 |
| I have difficulty expressing my thoughts | Valid Percent | 42.9 | 7.1 | 28.6 | 14.3 | 7.1 |
| I am bothered by the change in my personality | Valid Percent | 35.7 | 28.6 | 7.1 | 14.3 | 14.3 |
| I am able to make decisions and take responsibility | Valid Percent | 14.3 | 14.3 | 7.1 | 14.3 | 50.0 |
| I am bothered by the drop in my contribution to the family | Valid Percent | 21.4 | 28.6 | 7.1 | 21.4 | 21.4 |
| I am able to put my thoughts together | Valid Percent | 14.3 | 7.1 | 21.4 | 21.4 | 35.7 |
| I need help in caring for myself (bathing etc.) | Valid Percent | 78.6 | | | | 21.4 |
| I am able to put my thoughts into action | Valid Percent | 14.3 | 7.1 | 14.3 | 14.3 | 50.0 |
| I am able to read like I used to | Valid Percent | 28.6 | | 21.4 | 7.1 | 42.9 |
| I am able to write like I used to | Valid Percent | 21.4 | 7.1 | 14.3 | 7.1 | 50.0 |
| I am able to drive a vehicle | Valid Percent | 21.4 | | | 21.4 | 57.1 |

According to the results in Table 4.6 patients mostly did experience some changes in their QoL to various degrees. Areas of their life that seemed to be negatively affected was their ability to concentrate, their vision and hearing to some extent, being able to find the right words, putting their thoughts together and expressing their thoughts as well as the ability to read, write and drive a vehicle. This in turn affected their independence though most (78.6%) indicated that they did not need help in caring for themselves at all. While half (50%) of them have not experienced any seizures, 21.4% did a little bit, with 21.4% experiencing seizures quite a bit. Only 1 person (7.1%) experienced seizures very much. Patients were divided in their opinion regarding being able to remember new things,

getting frustrated that they could not do the things they used to and being bothered by the drop in their contribution to their families. A third of the patients (35.7%) indicated that they were not at all afraid of having a seizure, while the rest had some concern. A third (35.7%) was not bothered by the change in their personalities at all, while 28.6% did show a little bit of a concern. Just more than a third did show some concern regarding this issue. Most of the respondents (64.3%) indicated that they were able to make decisions and take responsibility, while 28.6% only felt so a little bit or not at all. Most patients felt that they were able to put their thoughts into actions in varying degrees.

The results in Table 4.7 once again gives an indication that there was mixed experiences with regards to the issues mentioned in this section relating to experiences of QoL. Approximately a third of the patients indicated that they never or almost never have been upset about things happening unexpectedly, were unable to control the important things in their lives, that they felt nervous and stressed or that they were angry because things were outside of their control. The remainder of the patients did, however, experience these feelings in varying degrees. Most of the patients felt confident in their ability to handle personal problems and that things were going their way. Almost a fifth (23.1%), did not feel that things were going their way. Almost half of the patients (46.2%) almost never felt as if they could not cope with the things they had to do, whilst the remained did battle with this in varying degrees. Most were able to control irritations in their lives and felt that they were on top of things. A third (30.8%) did, however, indicate that they never or almost never felt on top of things. Half of the patients (50%) indicated that they never or almost never felt that difficulties were piling up so high they could not overcome them. The remainder felt that that was the case in varying degrees.

According to these findings, the patients that responded in this survey clearly show numerous changes in their QoL in their ADL's. They are coping in most cases, but they experience an impact on their usual activities due to the illness. As the illness may progress and the treatment steps in, they will in the end experience more frustrations due to changes in their ADL's. The overall symptom burden and disability for glioma patients' quality of life are significant, especially in those with high-grade or recurrent disease. The difference in QoL may be less dependent on the grade of the tumor and more dependent on whether the tumor is

progressive or stable (Liu *et al.*, 2008). There are numerous amounts of aspects that influence QoL, as stated before, but symptoms that influence a different realm of QoL that shows difficulty in emotional and cognitive dimension. All of these changes in the patient may cause further anxiety and stress, due to the lack of the necessary information of the symptoms of this disease.

Table 4.7 : Results of responses on questions pertaining to quality of life (Continued)

| QUALITY OF LIFE | | Never | Almost never | Sometimes | Fairly often | Very often |
|---|---------------|-------|--------------|-----------|--------------|------------|
| How often have you been upset because of something that happened unexpectedly? | Valid Percent | 7.7 | 23.1 | 38.5 | | 30.8 |
| How often have you felt that you were unable to control the important things in your life? | Valid Percent | 7.7 | 30.8 | 30.8 | 7.7 | 23.1 |
| How often have you felt nervous and stressed? | Valid Percent | 7.7 | 30.8 | 15.4 | 30.8 | 15.4 |
| How often have you felt confident in your ability to handle your personal problems? | Valid Percent | 7.7 | 7.7 | 23.1 | 23.1 | 38.5 |
| How often have you felt that things were going your way? | Valid Percent | 23.1 | 7.7 | 15.4 | 46.2 | 7.7 |
| How often have you found that you could not cope with the things you had to do? | Valid Percent | | 46.2 | 15.4 | 15.4 | 23.1 |
| How often have you been able to control irritations in your life? | Valid Percent | 7.7 | 15.4 | 30.8 | 30.8 | 15.4 |
| How often have you felt that you were on top of things? | Valid Percent | 15.4 | 15.4 | 23.1 | 15.4 | 30.8 |
| How often have you been angry because of the things that were outside of your control? | Valid Percent | 23.1 | 7.7 | 30.8 | 23.1 | 15.4 |
| How often have you felt difficulties were piling up so high that you could not overcome them? | Valid Percent | 25.0 | 25.0 | 16.7 | 16.7 | 16.7 |

Quality of life is an important area of clinical neuro-oncology that is increasingly relevant as survivorship increases and as patients experience potential morbidities associated with new therapies (Liu *et al.*, 2008). The review of QoL studies in brain tumor patients shows the importance to share this knowledge for future research studies. Studies up to date about QoL have focused on specific symptoms like fatigue, sleep disorder and cognitive disorders, due to the fact that most cancer therapies are associated with these symptoms. There are however a need to establish a baseline and serial-quality-of-life parameters in brain tumor patients in order to plan and evaluate appropriate and timely interventions for their symptoms (Liu *et al.*, 2008)

4.3.3 Results of the correlation analysis between the indexes of physical, social, emotional and functional well-being and fatigue and quality of life

This section will focus on determining whether statistically significant relationships existed between the concepts measured by the indexes of the questionnaire. The following procedure was followed in determining the index scores.

- a) It was determined whether an index was positive or negative in the sense that high scores on a question were associated with a positive or negative trend. For example, I feel ill, if the patients indicated Very much it was in fact negative and if the majority of question in a particular scale was interpreted in this manner it was considered a negative scale. High scores in this case, were thus indicative of poor health.
- b) All questions were the ratings gave the opposite trend as that of the scale, were re-coded so that high and low scores are interpreted in the same manner.
- c) The responses of all the questions in the index were added together for each patient in order to obtain their index score on that construct.

The indexes that were calculated were as follows:

- a. Physical Well-Being: This index was calculated by the summation of questions 1 to 7 of the questionnaire. None of the questions needed to be recoded and the scale was considered a negative scale as high scores were associated with lower Physical Well-being.

- b. Social Well-being: This index was calculated by the summation of questions 8 to 14 of the questionnaire. None of the questions needed to be recoded and the scale was considered a positive scale as high scores were associated with higher Social Well-being.
- c. Emotional Well-being: This index was calculated by the summation of questions 15 to 20 of the questionnaire. Question 16 was recoded. The scale was considered a negative scale as high scores were associated with lower Emotional Well-being.
- d. Functional Well-being: This index was calculated by the summation of questions 21 to 27 of the questionnaire. None of the questions needed to be recoded and the scale was considered a positive scale as high scores were associated with higher Functional Well-being.
- e. Fatigue: This index was calculated by the summation of questions 28 to 40 of the questionnaire. Questions 34 and 35 were re-coded. The scale was considered a negative scale as high scores were associated with more Fatigue.
- f. Quality of Life: This index was calculated by the summation of questions 41 to 59 of the questionnaire. Questions 41, 43, 47, 49, 52, 54, 56, 57 and 58 were re-coded. The scale was considered a negative scale as high scores were associated with poorer perceptions of Quality of Life.

Table 4.8 contains the results of the *Spearman Rank-order correlations*. These results can be summarised as follows:

- a. There was a strong positive correlation ($r=0.789$; $p=0.001$) between Physical and Emotional Well-being. Both indexes were positive and indicated a strong association between Physical and Emotional well-being where better physical health was associated with better emotional health and *visa versa*.
- b. There was a strong negative correlation ($r=-0.747$; $p=0.002$) between Physical and Functional Well-being. Due to the fact that one index was positive and the other negative; this correlation coefficient should be interpreted in the following manner. There was a strong association between Physical and Functional well-

being, where better Physical Well-being was associated with better Functional Well-being.

- c. There was a strong positive correlation ($r=0.849$; $p=0.000$) between Physical Well-being and Fatigue. Since both indexes were negative this was indicative of a strong association between Physical and Fatigue, where better Physical Well-being was associated with less Fatigue.
- d. There was a strong positive correlation ($r=0.761$; $p=0.002$) between Physical Well-being and perceptions of QoL. Since both indexes were negative this was indicative of a strong association between Physical Well-being and perceptions of QoL. The better patients' Physical Well-being, the better their perceptions of their QoL.
- e. A moderate to strong negative correlation was found between Emotional and Functional Well-being ($r=-0.551$; $p=0.051$). This was however, only significant at the 10% level of significance. As the one index was positive and the other one negative, this correlation coefficient should be interpreted as follows: Better Emotional Well-being is associated with better Functional Well-being.
- f. There was a strong positive correlation between Emotional Well-being and Fatigue ($r=0.757$; $p=0.007$). Due to the fact that one index was positive and the other negative; this correlation coefficient should be interpreted in the following manner. There was a strong association between Emotional Well-being and Fatigue, where better Emotional Well-being was associated with less Fatigue.
- g. A strong positive correlation ($r=0.571$; $p=0.042$) existed between Emotional Well-Being and QoL. As both indexes were negative this was indicative of the fact that higher Emotional Well-being was associated with better perceptions of Quality of Life and the visa versa.
- h. There was a strong negative correlation ($r=-0.652$; $p=0.022$) between Functional Well-being and Fatigue. As one index was positive and the other negative, this was indicative of the trend that better Functional Well-being was associated with less Fatigue.
- i. The same trend was found between Functional Well-being and perceptions of Quality of Life with a strong negative correlation of ($r=-0.857$; $p=0.000$). Higher

levels of Functional Well-being, was thus associated with better perceptions of Quality of Life.

- j. Fatigue scores was also strongly correlated to Perceptions of Quality of Life with a strong positive correlation of ($r=0.736$; $p=0.006$). As both indexes were negative this was indicative thereof that higher Fatigue scores were associated with poorer perceptions of Quality of Life and visa versa.

Table 4.8 : Correlations between indexes of well-being

| | | | Physical Well-being | Social Well-being | Emotional Well-being | Functional Well-being | Fatigue | Quality of Life |
|-----------------|-------------------------|-------------------------|---------------------|-------------------|----------------------|-----------------------|---------|-----------------|
| Spearman's rho | Physical Well-being | Correlation Coefficient | 1.000 | -.359 | .789** | -.747** | .849** | .761** |
| | | Sig. (2-tailed) | . | .279 | .001 | .002 | .000 | .002 |
| | | N | 14 | 11 | 13 | 14 | 12 | 14 |
| | Social Well-being | Correlation Coefficient | -.359 | 1.000 | -.370 | .103 | -.313 | -.234 |
| | | Sig. (2-tailed) | .279 | . | .262 | .764 | .412 | .489 |
| | | N | 11 | 11 | 11 | 11 | 9 | 11 |
| | Emotional Well-being | Correlation Coefficient | .789** | -.370 | 1.000 | -.551 | .757** | .571* |
| | | Sig. (2-tailed) | .001 | .262 | . | .051 | .007 | .042 |
| | | N | 13 | 11 | 13 | 13 | 11 | 13 |
| | Functional Well-being | Correlation Coefficient | -.747** | .103 | -.551 | 1.000 | -.652* | -.857** |
| | | Sig. (2-tailed) | .002 | .764 | .051 | . | .022 | .000 |
| | | N | 14 | 11 | 13 | 14 | 12 | 14 |
| Fatigue | Correlation Coefficient | .849** | -.313 | .757** | -.652* | 1.000 | .736** | |
| | Sig. (2-tailed) | .000 | .412 | .007 | .022 | . | .006 | |
| | N | 12 | 9 | 11 | 12 | 12 | 12 | |
| Quality of Life | Correlation Coefficient | .761** | -.234 | .571* | -.857** | .736** | 1.000 | |
| | Sig. (2-tailed) | .002 | .489 | .042 | .000 | .006 | . | |
| | N | 14 | 11 | 13 | 14 | 12 | 14 | |

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

4.3.4 Results of the analysis of statistically significant differences between patients who exercised versus those who did not on all index scores

The main aim of the analysis was to determine whether statistically significant differences existed between patients who did exercise versus those who didn't on all the indexes calculated. The analysis was repeated for both Strenuous, Moderate and Mild exercise, prior to diagnosis, during treatment and after treatment. The complete analysis can be found in Appendix B. Mann-Whitney U-tests were used to do the analysis due to the small base size.

Only one statistically significant difference was found. There was a statistically significant difference between patients who participated in strenuous exercise before diagnoses and those who didn't in terms of perceptions of Quality of Life ($p=0.034$). The QoL index was negative thus higher scores were associated with poorer perceptions of quality of life. The mean scores indicated that those patients who did participate in strenuous exercise prior to diagnoses had significantly higher scores than those who did not participate in strenuous exercise. The implication is that they have poorer perceptions of their current Quality of Life than those who did not exercise.

Patients being diagnosed with cancer often experience psychological outfall after diagnosis and starting with treatment and they found the disease is synonymous with an inactive lifestyle, which result in loss of muscle mass and strength (Adamsen *et al.*, 2009). Another recent study showed that exercise improves physical performance in cancer patients undergoing myeloablative therapies (Dimeo, 2001). In a study done on cancer patients by McNeely *et al.* (2006) three studies provided adequate data to assess QoL. The pooled estimate showed that statistically significant increase of greater than 4.0 point on the FACT scale representing a clinical meaningful improvement in QoL from exercise. Taking these literatures into account, patients that are more active will show a higher level of QoL than patients with an inactive daily lifestyle.

Exercise appears to result in an improvement of the physiologic parameters observed, included increases in functional capacity and lean tissue, decrease in percent body fat, nausea and fatigue. It also shows an improvement in psychological indicators of well-being and quality of life (Freidenreich & Courneya, 1999).

No other statistically significant differences were found in this study, however, especially during treatment, very few patients exercised which influenced the analysis and this could be addressed with future studies, if a larger sample was possible. It would allow better differentiation in terms of participation in exercise.

4.3.5 Results of the analysis of patients' participation in sport and exercise preferences

The results in Figures 6 to 8 give an indication of the number of times that patients exercised prior to diagnosis, during and after treatment. The time spent exercising can be viewed in Appendix A. Figures 4.9 to 4.17 give an indication of patients exercise preferences. Patients' perceptions of exercise are presented in Table 4.9. Table 4.10 gives an indication of the support and approval that patients felt they would receive to exercise regularly over the month following the survey.

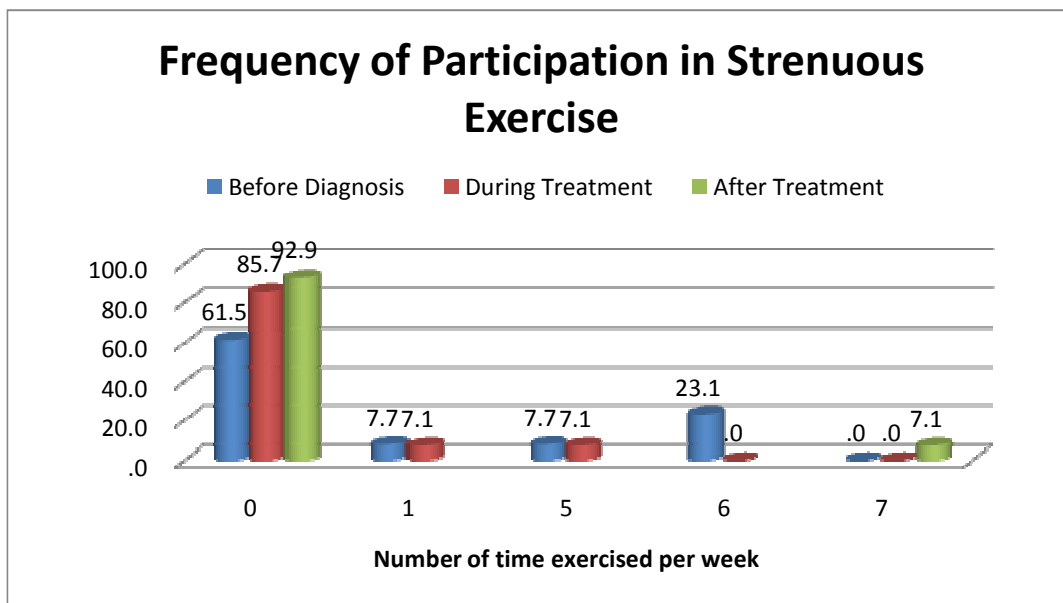


Figure 4.6 : Participation in strenuous exercise by participants

It is clear from Figure 4.6 that more than half of the patients (61.5%) did not take part in strenuous exercise prior to diagnosis. This number increased to 85.7% during treatment and 92.9% after treatment. The minority of patients thus participated in strenuous exercise. Before diagnosis 23.1% did exercise 6 times per week with 1 or no patients participating in exercise between 1 and 7 times a week.

There is a considerable rationale for promoting multimodal exercise interventions to improve physical capacity, vitality, and physical and mental well-being and to relieve fatigue during chemotherapy; thereby supporting cancer patients' daily living activities. In the study done by researchers, they used high intensity exercise intervention on cancer patients that included aerobic exercises, strength training and relaxation exercises that would be equivalent to a total of 45 MET (Metabolic equivalent of task) per week (Adamsen *et al.*, 2009). According to the study Adamsen *et al.* (2009) most participants were not in an advanced part of cancer, so exercise did boost them physically, emotionally, psychosocially. In this study it definitely showed that strenuous exercise is not the correct way to go with a brain cancer patient. As seen on Figure 4.6, all participants had reduced exercise intensity and this just shows how they had to adapt to the lifestyle changes that they had to make due to the illness.

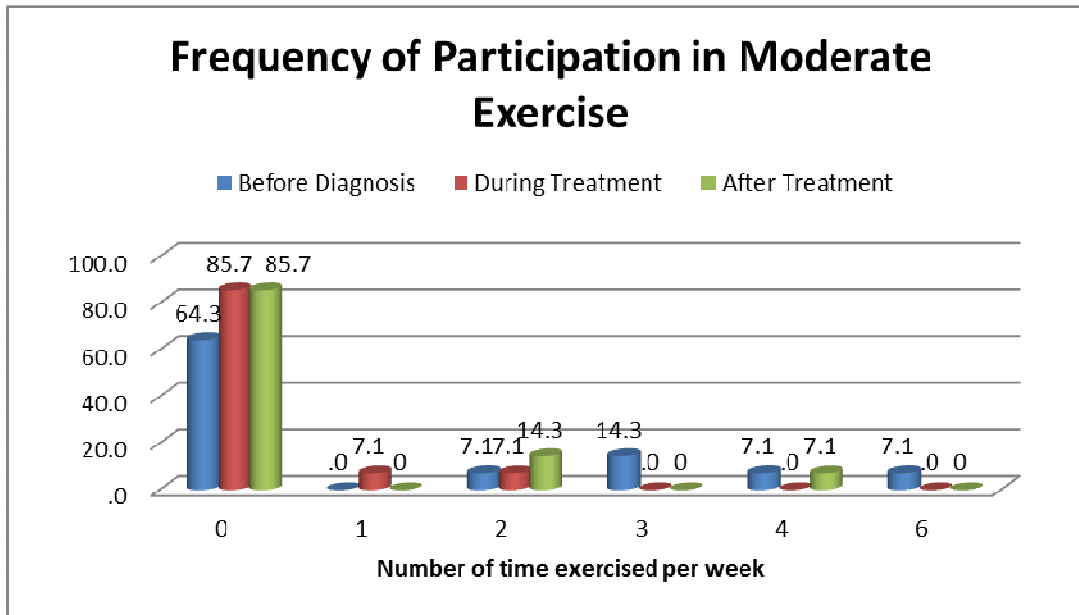


Figure 4.7 : Participation in moderate exercise by participants

Once again two thirds (64.3%) of patients did not exercise moderately prior to diagnosis and this figure increased to 85.7% during treatment and after treatment. Slightly more patients participated in moderate exercise twice a week when compared to the strenuous exercise.

Due to the fact that cancer-related fatigue plays such an enormous part in cancer treatment, the idea of physical exercise is still in some areas a novelty that has struggled to gain acceptance. In the above table it shows that more participants did participate in moderate exercise programs versus strenuous exercises. A multicenter, randomized controlled trial did a study on cancer individuals with the goal of determining the effect of home-based walking exercise program on fatigue, emotional distress and QoL (Stasi *et al.*, 2003). Home-based exercises are usually moderate to light exercises due to the fact that the patient controls the intensity of the exercises. Moderate to light exercises may be more effective than continuous rest, therefore walking exercises that are moderate of nature can increase overall muscle tone, relieve emotional distress and help with ADL (Stasi *et al.*, 2003).

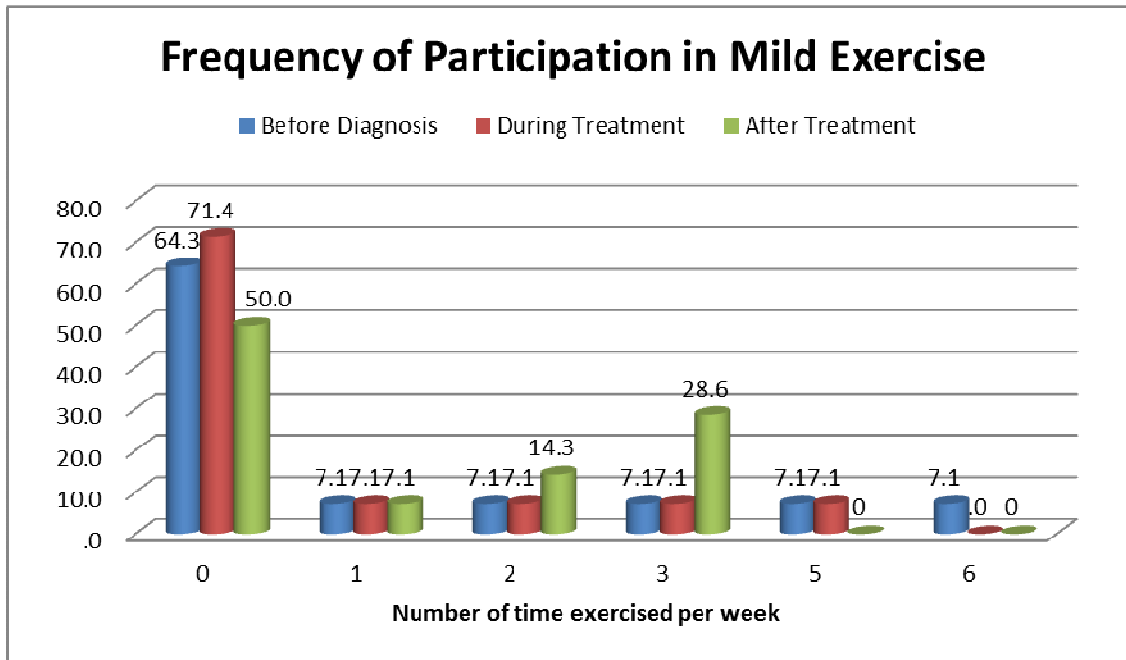


Figure 4.8 : Participation in mild exercise by participants

Two thirds (64.3%) of patients did not participate in mild exercise prior to diagnosis. This number increased to 71.4% during treatment, but after treatment only half of the patients (50%) indicated that they did not exercise mildly. More patients exercised twice a week with 28.6% exercising 3 times per week after treatment. Compared to the strenuous and moderate exercises, more patients participated in mild exercise especially after treatment.

Mild exercising does not mean that you would have to participate in a gym or prescribed program, but it merely means that you can do plain house work or walk in the garden or just being mobile. It is beneficial due to the fact that many cancer survivors still exercise regularly at home, community centers, or health clubs as members. In the survey it showed that patients engaged in a walking program, which falls under mild to moderate exercise, were done by 59-71% of the participants (Durak *et al.*, 2001). According to Wiggins (2004) physical fitness can be increased at lower levels of exercise intensity. The belief therefore is that any exercise, mild or moderate, is better than rest or inactivity. The hypothesis of Durak *et al.* (2001) was that not only is exercising safe, but

that it will show substantial improvements in QoL measures independent of place of exercise or instructional methods implemented.

The general exercise prescription for people undertaking or having complete cancer therapy is low to moderate intensity, regular frequency (three to five times a week) for at least 20 minutes per session, involving aerobic, resistance or mixed types (Velthuis *et al.*, 2009).

In another study a significant association existed at lower walking levels, with minimal benefits also being found for moderate-paced walking for 3 hours per week. These investigators found that walking was the most preferred activity for sedentary adults talking up activity, and acknowledged that a benefit of taking up a walking programme might be the best for being active (Windsor *et al.*, 2009).

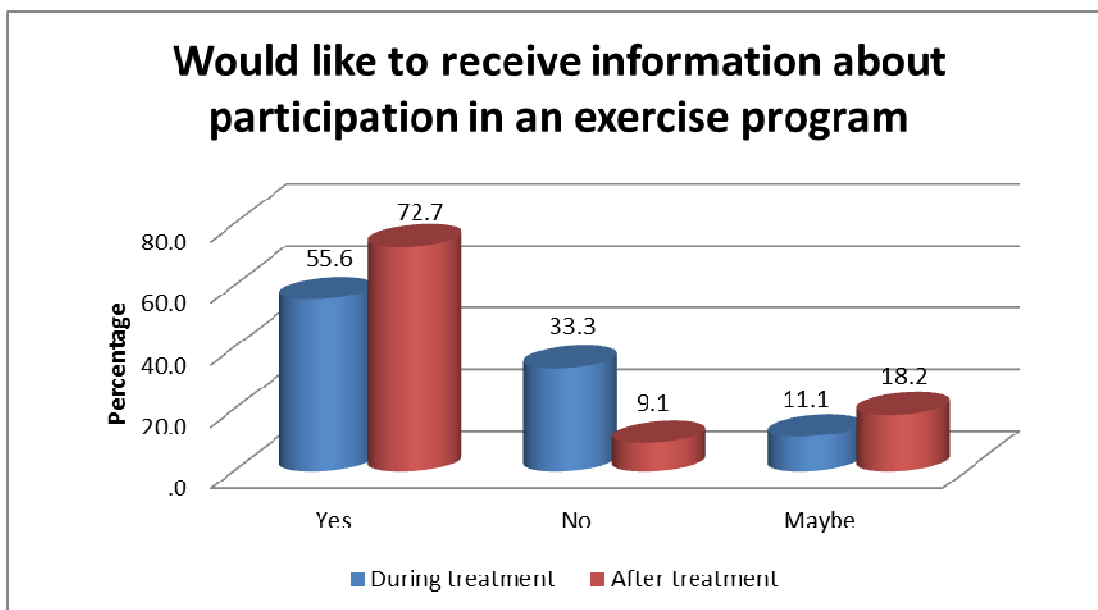


Figure 4.9 : Necessity of receiving information about exercise programs

Most of the patients (72.7%) would like to receive information about exercise programs after treatment, while half (55.6%) would like to receive this information during treatment. A third (33.3%) of the patients was not interested in receiving this information during

treatment. Between 11.1% and 18.2% indicated that they would maybe like to receive information regarding exercise programs during or after treatment respectively.

A result of survey done by researchers, physicians are aware that their patients engaging in exercise (78%) and most are highly supportive of the patients' participation (98%) (Durak *et al.*, 2001). It is important that physicians are supportive of these exercise programs due to the fact that patients will find comfort in the fact that physicians know the benefits of exercise and that is safe to participate in such an intervention.

In a study done by Windsor *et al.* (2009), they found that the provision of information regarding exercise as well as fatigue was well received by patients.

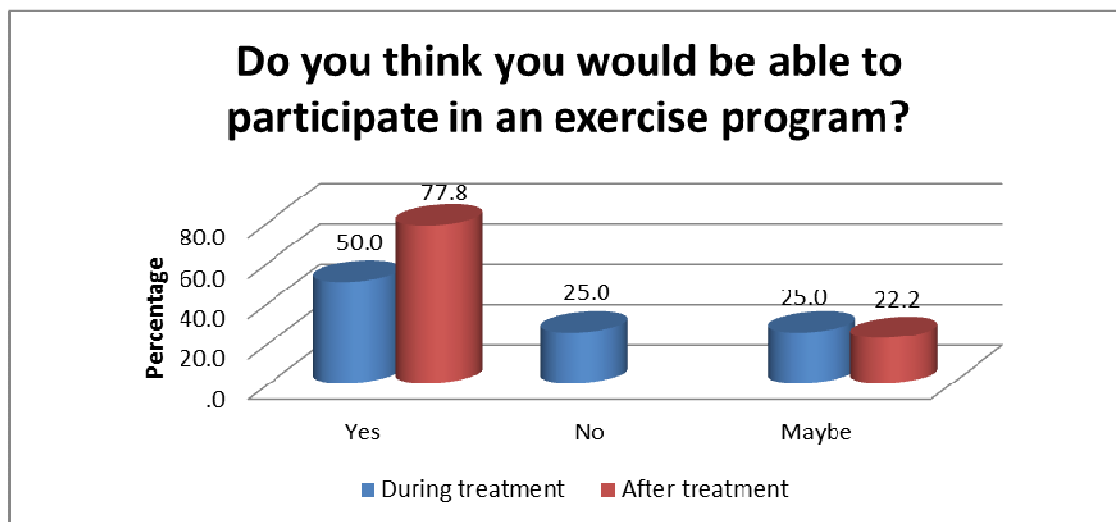


Figure 4.10 : Participants that will participate in an exercise program

Most of the patients (77.8%) indicated that they would be able to participate in an exercise program after treatment compared to 50% who indicated that they would be able, during treatment. A quarter indicated that they would not be able to exercise during treatment with another 25% indicating that they would maybe be able to do it. None of the patients indicated that they would not be able to exercise after treatment.

The reduction in usual physical activity and exercise following the diagnosis and the treatment of cancer has been well documented, often resulting in physical deconditioning and functional decline (Ingram & Visovsky, 2007). In brain cancer patients like Glioblastoma Multiforme, QoL is initially shorter after treatment. The shorter stable QoL is due to the briefer time to tumor progression and neurocognitive deterioration (Brown *et al.*, 2006). Therefore the functional decline will be more rapid than those of other cancer patients. Inactive will influence the ADL and QoL of these patients tremendously. Brain tumor patients' QoL scores will be low, but still be able to do some kind of exercise that is of a very low intensity. Another fact though is that most cancer survivors do not resume their pre-diagnosis activity levels following treatment even if they are physically able to do so (Ingram & Visovsky, 2007).

In a study done by Hayes *et al.* (2011), the Exercise Physiologist supported the patients with expertise exercise intervention, but they gave them the freedom to decide what works for the patient.

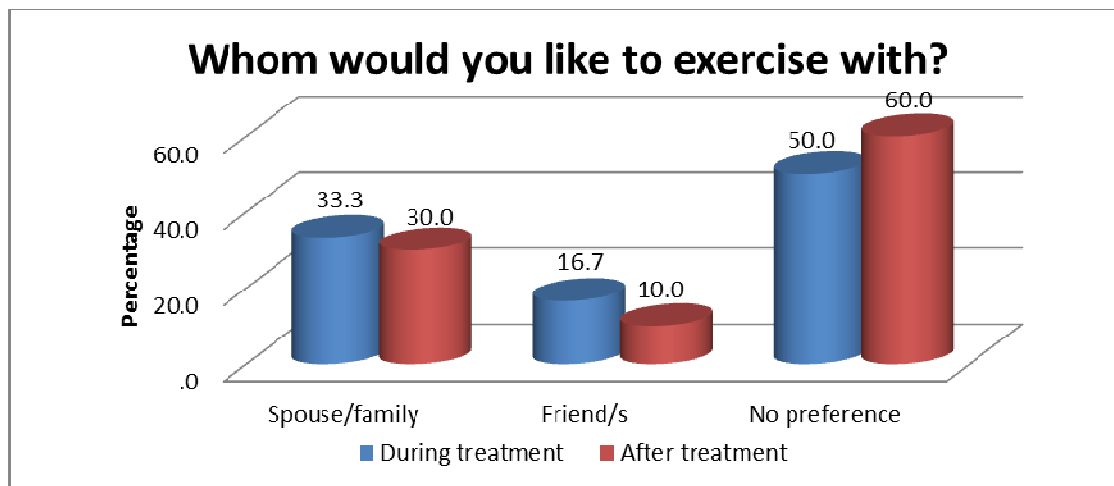


Figure 4.11 : Preference of company to exercise with during illness

Most of the patients did not have a preference with whom they would like to exercise either during (50%) or after treatment (60%). Spouses or family were selected by a third of the patients with the remainder indicating that they would prefer to exercise with friends (see Figure 4.11).

Home-based exercises that were researched by scientists like Durak (2001), Stasi *et al.* (2003), Windsor *et al.* (2009), and Velthuis *et al.* (2009) have proved that most cancer patients prefer to exercise with close friends or their spouse.

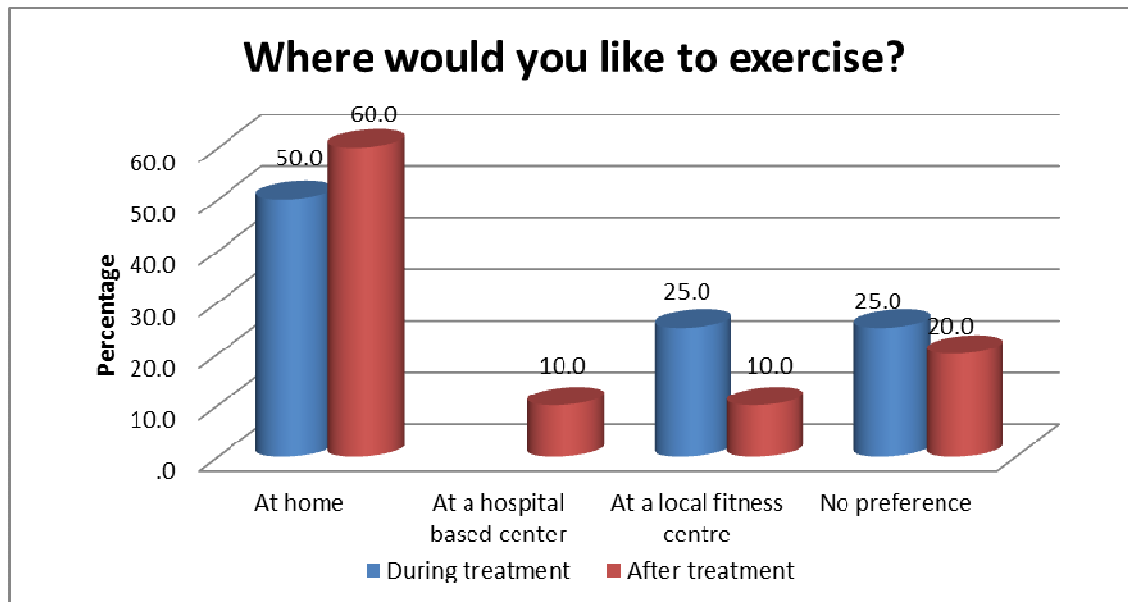


Figure 4.12 : Preference of where to exercise

According to the results in Figure 4.12, most of the patients would like to exercise at home either during (50%) or after treatment (60%). Twenty (20%) to 25% indicated no preference with another 25% indicating that they would like to exercise at a local fitness center during training. 10% of patients indicated that they would either like to exercise at a hospital based center or a local fitness center after treatment.

In most studies, home-exercise interventions that consist mostly of walking and sometimes combined with resistance training, the patients' intensity varied "at own desired" pace and 70% of maximal heart rate (MHR) (Velthuis *et al.*, 2009). This means the 50% in this study that preferred home-based exercises have the same idea of exercising at own pace. Whereas the supervised type of exercise like in a fitness center or hospital based center, the patients will be monitored and they need to keep up to the pace that the therapist or physician favor.

In a randomized controlled study among men with prostate cancer, men randomized to aerobic exercise, did low-moderate walking program that was home-based during a period of 4-weeks whereas been under radiotherapy. This group of men has shown a significant improvement in physical functioning, even while receiving radical external beam radiotherapy and also shown no significant increase in fatigue during this period.

In a study where written information on fatigue and exercise was provided to patients starting with cancer treatment, where encouraged to engage in physical activity during their cancer treatment using walking or home-based exercise, to maintain their daily living activities (Windsor *et al.*, 2009). Through all these literature, it mostly shows that most patient will prefer home-based exercises at own pace. Windsor also stated in their study that the patients rather do a walking programme at home than a supervised exercise classes.

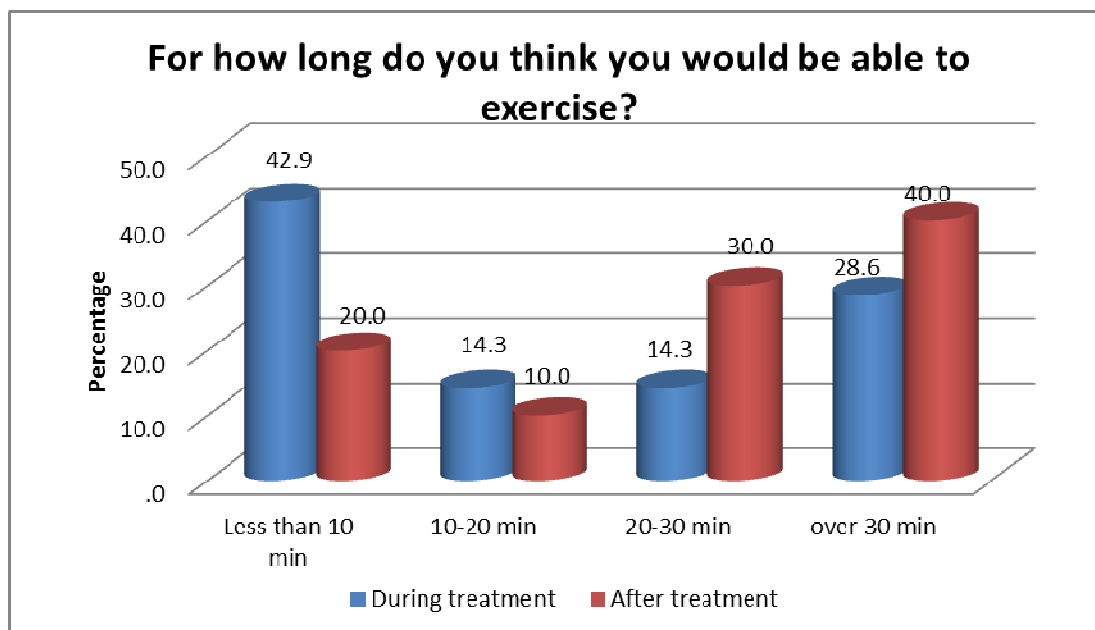


Figure 4.13 : Preference of duration of exercise session/program

The results in Figure 4.13 indicated that patients thought that they would be able to exercise much longer after treatment than during treatment. Almost half (42.9%) indicated that they would be able to exercise for less than 10 minutes during treatment

compared to 20% after treatment. 70% of patients indicated that they would be able to exercise between 20-30 minutes or more than 30 minutes after treatment.

Due to the fact that home-based exercises were mostly preferred among cancer patients, the pace they want to keep will be their own. Walking programmes that was the preference as well, suggested that they will at the most exercise for 20-40 minutes at the most. In the study by Windsor *et al.* (2009) the patients also commented on their use of daily living activities for exercise, such as gardening or housework. This still means that the patient will exercise at own pace till feeling fatigued.

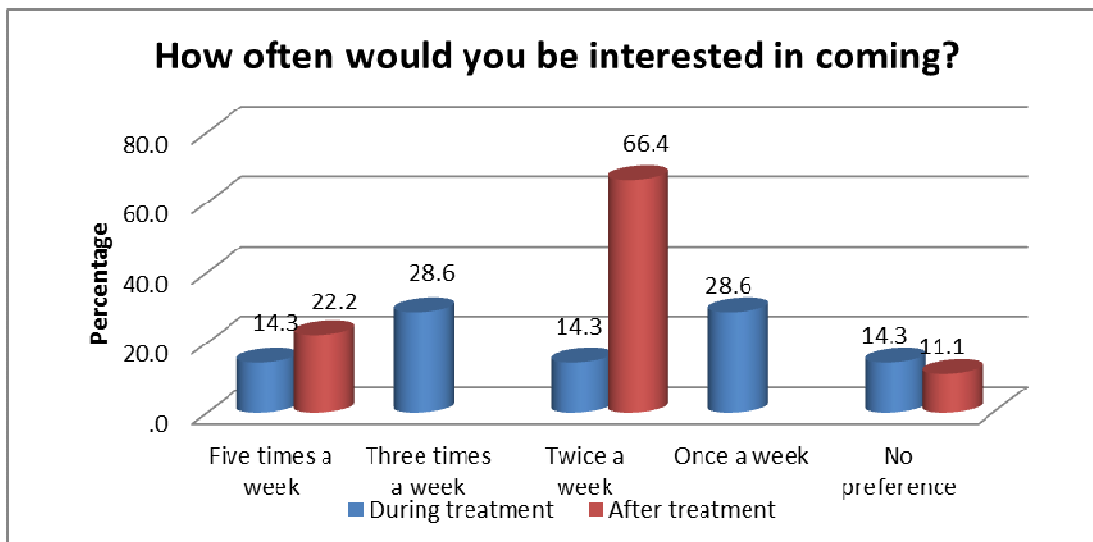


Figure 4.14 : Preference of frequency of exercise program

Most of the patients (66.4%) would be interested to exercise twice a week after treatment. Twenty two point two percent (22.2%) would like to exercise 5 times per week after treatment. During treatment 28.6% of patients would like to exercise once a week or 3 times a week respectively.

In studies of patients with cancer, participants exercised anywhere from 3 to 7 days a week, 10 to 45 minutes per session at 50% to 85% of heart rate reserves (Young-McCaughan & Arzola, 2007). This means that the most patients' intensity and frequency of exercise will depend on their overall well-being at that given time as well as

from the stage of treatment they are in. It could be difficult to participate in an exercise program while undergoing cancer treatment according to a study done by Young-McCaughan *et al.* (2003) in Frontera, (2006).

4.3.6 Results of the analysis of patients' beliefs regarding exercise and their intention of exercise in coming months

Table 4.9 : Perceptions of exercise and how it will impact on their daily life and overall well-being

| Perceptions of exercising regularly over the next month | | Extremely unenjoyable | Slightly unenjoyable | Neither | Slightly enjoyable | Quite enjoyable | Extremely enjoyable |
|---|---------------|-----------------------|----------------------|---------|----------------------|-------------------|-----------------------|
| Unenjoyable vs. Enjoyable | Valid Percent | 8.3 | 8.3 | 16.7 | 8.3 | 50.0 | 8.3 |
| | | Extremely harmful | Quite harmful | Neither | Slightly beneficial | Quite beneficial | Extremely beneficial |
| Harmful vs. Beneficial | Valid Percent | | | 8.3 | | 50.0 | 41.7 |
| | | Extremely boring | Quite boring | Neither | Slightly interesting | Quite interesting | Extremely interesting |
| Boring vs. Interesting | Valid Percent | | | 8.3 | 16.7 | 50.0 | 25.0 |
| | | Extremely foolish | Quite foolish | Neither | Slightly wise | Quite wise | Extremely wise |
| Foolish vs. Wise | Valid Percent | | | | | 50.0 | 50.0 |
| | | Extremely unpleasant | Quote unpleasant | Neither | Slightly pleasant | Quite pleasant | Extremely pleasant |
| Unpleasant vs. Pleasant | Valid Percent | | | 8.3 | 16.7 | 50.0 | 25.0 |
| | | Extremely bad | Quote bad | Neither | Slightly good | Quite good | Extremely good |
| Bad vs. Good | Valid Percent | | | | | 41.7 | 58.3 |

The results in Table 4.9 mostly indicate a positive attitude and beliefs regarding exercise in the month following the survey. All the patients indicated that it would be quite or extremely wise and good for them to exercise in the month following the survey. Most also indicated that it would be beneficial, interesting and pleasant to exercise. Fewer patients felt that it would be enjoyable, with 16.6% indicating that they would find it extremely or slightly unenjoyably.

Table 4.10 : Perceptions of support and approval from others regarding exercise.

| Perceptions of support and approval regarding exercise | | Strongly disagree | 2 | 3 | 4 | 5 | 6 | Strongly agree |
|--|---------------|-------------------|---|-----|---|------|------|----------------|
| Most people who are important to me think I should exercise regularly over the next month | Valid Percent | 8.3 | | | | 16.7 | 16.7 | 58.3 |
| Most people who are important to me would encourage me to exercise regularly over the next month | Valid Percent | | | 8.3 | | 8.3 | 25.0 | 58.3 |
| Most people who are important to me would approve of me exercising regularly over the next month | Valid Percent | | | | | 16.7 | 8.3 | 75.0 |

Only one person (8.3%) who answered this question indicated that they strongly disagreed that most people who were important to them thought that they should exercise regularly over the following month. In most cases patients seemed to have support, encouragement and approval from significant others to exercise regularly over the following month (see Table 4.10).

In a study by Windsor *et al.* (2009) there was a nursing intervention that using individualized education of patients with cancer that decreased their perception of fatigue. Information and instructions was found to help patients undergoing radiotherapy maintaining their usual daily living activities.

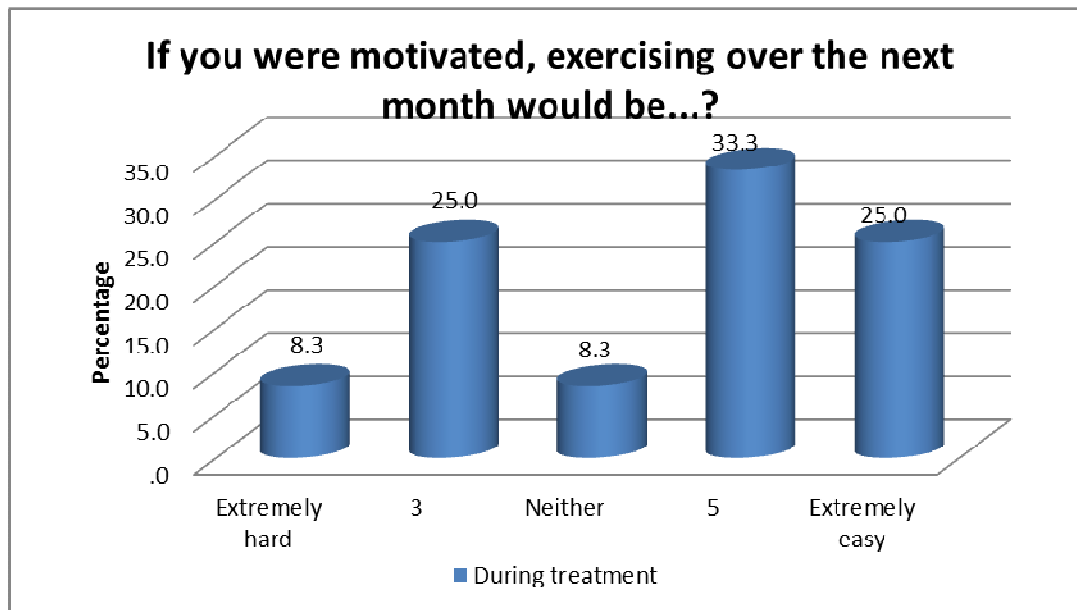


Figure 4.15 : Motivation of exercise participation

More than half of the patients (58.3%) indicated that they would find it easy to exercise over the month following the survey. A third (33.3%) indicated that it would be hard for them see Figure 4.15).

Due to the fact that the participants in this study were positive regarding exercise as an intervention, they sure did show it. Over 50% believed that exercising in the month after treatment would be quite easy. In this study almost 50% of the patients were still in a full time working situation. This means, still active and this will also help emotionally with the coping with the disease, exercise and other ADL matters.

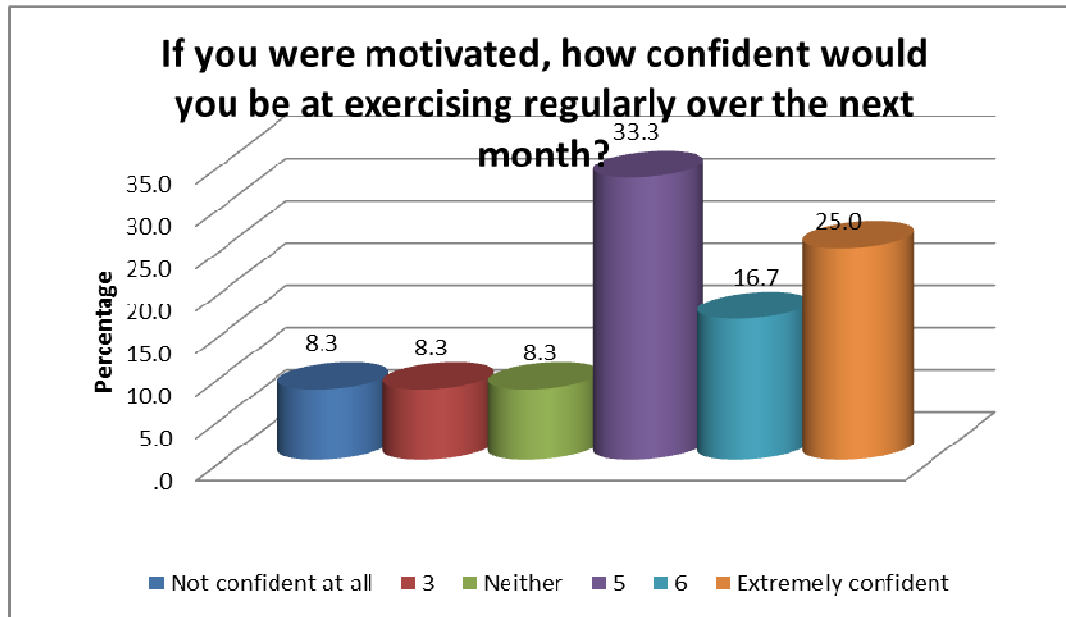


Figure 4.16 : Confidence of patient to participate regularly in exercise sessions

Most patients indicated that they were confident to exercise in the month following the survey. Due to the high rate in confidence in this study, it shows that patients will have the courage to do some physical activity even if it of low intensity. Physical activity does improve physical functioning overall. It is no wonder that the word “exercise” that derives from a Latin root meaning “to maintain”, “to keep”, “and to ward off” will improve confidence in life overall. (Kramer, 2003). I believe it is important to them to keep as much independence as possible for as long as possible

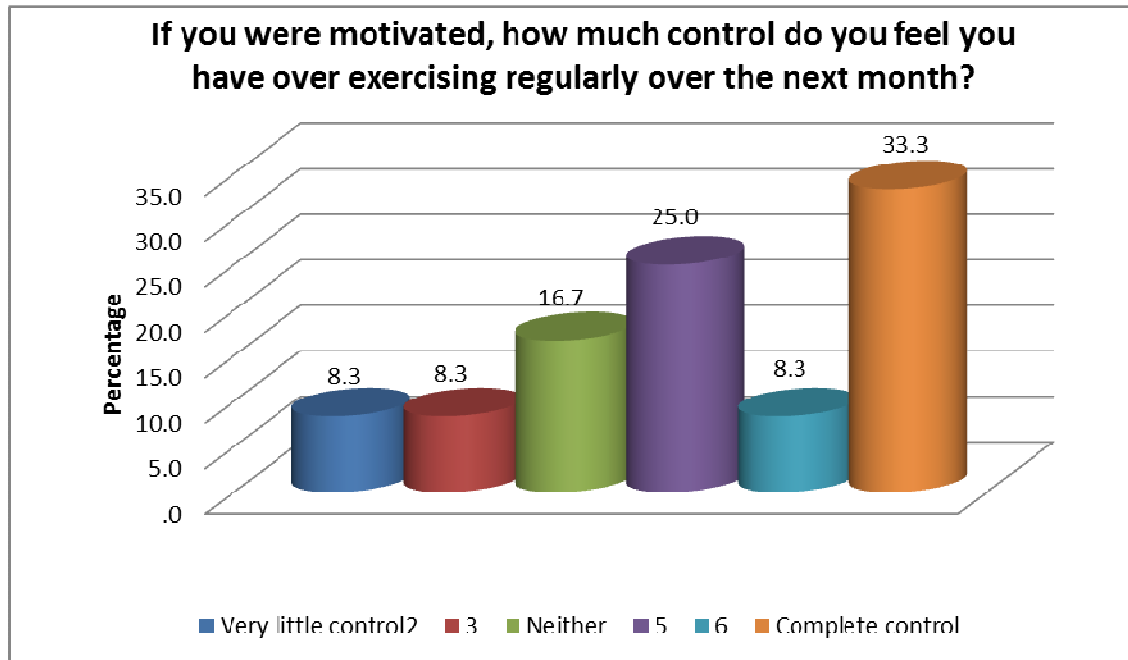


Figure 4.17 : Confidence of the patient’s control over physical activity

Most of the patients (87.6%) felt that they would be in control to exercise over the month following the survey (see Figure 4.17).

Exercise modulates both plasticity and various supporting systems that participate in maintaining brain function and health (Cotman *et al.*, 2007). Through this literature study it shows that exercise impacts on the brain on a very positive manner. To have control over your emotional health as well as over physical functioning will positively impact on the brain tumor patient. The emotional- and physiological well-being will definitely impact on how the patient will respond to physical activity.

4.3.7 Patients' preferences regarding the media they prefer for receiving information regarding exercise programs

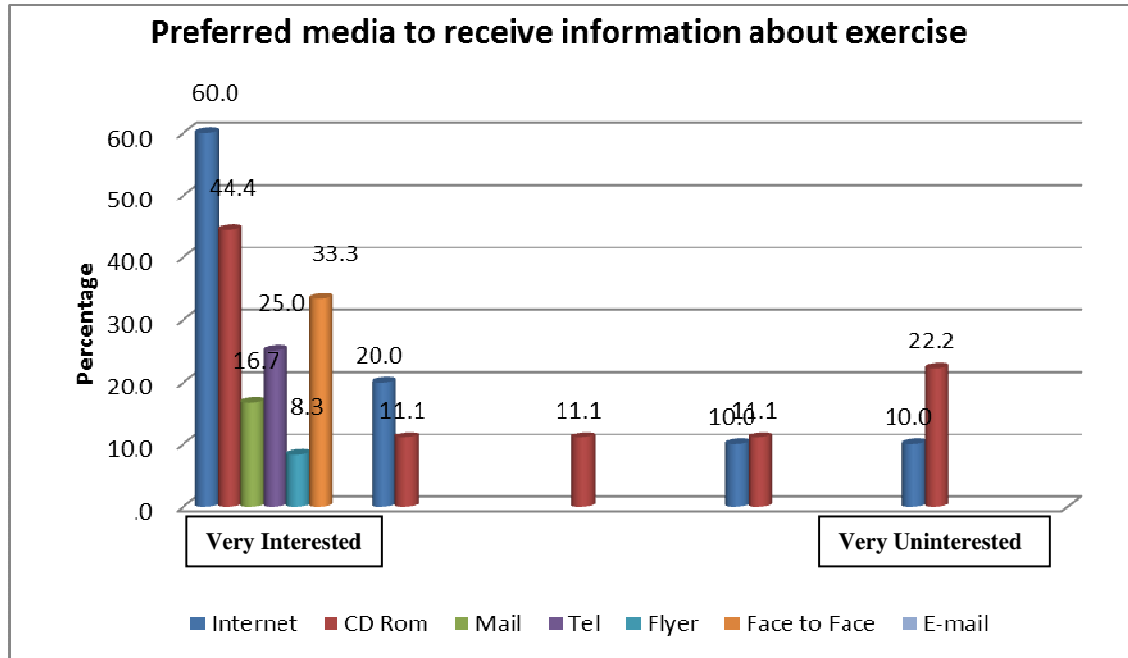


Figure 4.18 : Preference of through which media to be contacted with

More than half (60%) of the respondents indicated that they would be interested to receive information regarding exercise programs via the Internet, followed by 44.4% who prefer CD Rom and 33.3% who prefer face to face. A quarter (25%) preferred receiving this information via telephone and 16.7% via posted mail. E-mail was the least preferred media. According to my own experience, most people like to be faced when discussing important issue. The patient or person will read the facial expression, as well as the body language of the doctor the clinical specialist to give and indication of the seriousness of the situation or it could give them comfort or reassurance. Email, phone calls and flyers are impersonal.

In nowadays, the first line of information to give patients advice on handling cancer needs to be the physician that treats the patient. A booklet, cd or a councilor will in most cases will ease some of the patient's fears. Telephone conversations are in many cases irritating to people and emails are totally impersonal.

4.4 SUMMARY OF RESULTS

As indicated earlier, the sample consisted of 14 patients with Primary Brain Cancer. More than half of them were married, with a third who had high school diplomas or graduate level qualifications respectively. Half of the patients were employed with 25% who indicated that they were disabled. Two thirds of the patients have smoked more than 100 cigarettes in their lifetimes, but 91.7% were not smoking at the time of the survey.

General perceptions of the Physical Well-being was fairly positive, where most patients indicated that they did not suffer or only suffered very little from the symptoms of the disease. Their perceptions of their Social and Emotional Well-being were also fairly positive. Functional Well-being was mostly perceived positively. Patient's perceptions of levels of Fatigue differed considerably, where half did not experience Fatigue and the rest experienced it in varying degrees. Mostly, patients did experience changes in their Quality of Life. Areas that seemed to be negatively affected was their ability to concentrate, their vision and hearing to some extent, their ability to find the right words or putting their thoughts together and expressing their thoughts as well as their ability to read, write and drive a car.

The results of the correlation analysis indicated that better Physical Well-being was significantly related to better Emotional and Functional Well-being and better perceptions of Quality of Life. Poorer Physical Well-being was associated with higher Fatigue. Better Emotional Well-being was strongly correlated to better Functional Well-being and better perceptions of Quality of Life. Higher Emotional Well-being scores were also associated with less Fatigue. High Fatigue was associated with poorer perceptions of Quality of Life.

The results of the analysis of statistically significant differences between those patients who did participate in sport versus those who didn't only showed one statistically significant difference. Patients who did participate in strenuous exercise prior to diagnosis experiences poorer perceptions of Quality of Life that those who didn't.

Mostly, patients tended not to exercise during treatment with an increase in activity thereafter.

Most patients would like to receive information about exercise programs after treatment with half who would also like to receive it during treatment. Most felt that they would be able to participate in such a program after treatment. Most patients showed no preference for who they would like to exercise with, but those who did have a preference, preferred their family or spouse. Patients mostly wanted to exercise at home. There was a general perception that they would be able to exercise for a longer duration after treatment than during treatment and that they would be interested to exercise twice a week. Patients mostly had a positive attitude and beliefs towards exercise. Exercising after treatment seemed to be supported and approved by others in their lives. More than half of the patients seemed motivated to exercise in the month following this survey. Most of them felt confident to exercise and that they had control over it for the following month. Most patients were interested to receive information regarding exercise programs via the internet.

4.5 DISCUSSION OF RESULTS

In this study a positive group of patients were recruited. In most cases they were positive towards exercise intervention, even though they were not always capable to perform them. They understood the positive influence of this intervention as an adjuvant therapy to cancer treatment.

To approach a patient holistically is very important to a Biokinetics. They need to focus on the physical-, psychological-, social- and emotional aspects. All of these different holistic aspects may influence the patient's injury or illness. Holistic approach equals quality of life. Quality of life will impact the total of the person's well-being.

Quality of life in the form of physical-, emotional-, social well-being is the most important area to sustain in any cancer patient. In this study there were a positive correlation between emotional- and physical well-being, which means that being physically active in

ADL's will help the patient to be more emotionally stable. In a study it was proved that exercise influence behavioral, for example to relieve stress, and can reduce depression and anxiety in humans (Cotman & Berchtold, 2002). Stress and emotions walk hand in hand. Emotions are a very powerful tool in human living. It usually defines a person's way of thinking. That it is so important for a brain tumor patient to be as positive as possible throughout the diagnosing and treatment phase.

Physical well-being and functional well-being also walks hand in hand in cancer therapy. Cancer-related fatigue is a very troublesome symptom in cancer therapy. It is therefore important to note that inactiveness actually increases levels of fatigue (Conn-Levin, 2005). In recent studies, physical exercise shows promise in preventing and reducing complaints of cancer-related fatigue (CRF). Physical activity tends to have positive impact on CRF. It was therefore proven that exercise is an intervention method for fatigue during cancer treatment (Windsor *et al.*, 2009). The correlation between emotional-, physical well-being and fatigue were positive. The statistics in this study are positive, meaning that being emotionally stable; physically active the cancer patient's fatigue levels will decrease significantly.

The correlation of quality of life and physical activity, which is the main objective of the study, shows a positive correlation. This indicates that physical activity or exercise will improve the QoL of the brain tumor patient. Exercise is safe and an efficacious intervention for cancer patients, independent on the location and instructional methods. Therefore, any exercise has a positive influence on the cancer patient, no matter where, when and how (Durak *et al.*, 2001). This means that exercise will definitely impact on the patient's physical well-being and emotional well-being. The growing body of research surrounding exercise in patients with cancer shows dramatic improvements in physiologic and psychological functioning in patient's participating in aerobic exercise programs (Young-McCaughan & Arzola, 2007).

Brain tumor patients are a different population of cancer patients. They represent a population with very low survival rates, with only a 19% survival of the disease for five

years or less. There has been no improvement in survival in the period since cancer registration began (www.cancersa.org.au, 2006).

The treatment of brain tumor patients depends on when the patient has been diagnosed, early or in the last stages. Higher grade brain tumors will last at least six months, where the last two months will be of no effect what so ever. This means that they will be either hospitalized or in palliative care. Therefore it is important to educate the patients when they are diagnosed and prepare them for exercise as an adjuvant therapy, even though it is only for a very short interval. In the last 20 years we had seen advances in the treatment of, and outcomes of brain tumor patients (Janda *et al.*, 2007).

Despite the fact that brain tumor patients does not have a very long survival time according to previous statistics, exercise can still have a positive influence on a brain tumor patient's health. Physical activity, such as walking or running on a treadmill, swimming, and weight-bearing exercise, is known to increase neural activity in both peripheral and central nervous system (Seo *et al.*, 2010). Brain tumor patients can improve overall physical strength and aerobic fitness, even if it only to cope with ADL's. Again, physical activity or exercise intervention for brain tumor patients is only to help these patients to extent their QoL for as long as possible.

CHAPTER 5

SUMMARY

5.1 INTRODUCTION

According to the studies conducted throughout the years, it is clear that the hope for brain tumor patients is quite slim. Although there are as much as 120 different types of tumors to the brain or CNS, it does appear that the prognosis remain dark in most cases. There is also a problem to conduct studies in the form of randomized controlled trials due to the fact that there will in most cases be problem to recruit brain cancer patients for a study that must range over a time period of a year. According to most literature studies primary brain tumor patients' survival rate will range mostly for 26 – 51 weeks at most.

Brain tumors can also not be predicted therefore, the overall fear of all people is what to look out for as possible early signs or medical conditions that may cause an illness like this. The only possible heredity condition is very rare named neurofibromatosis type 1 en 2, and this only accounts for 5 % of brain tumors. Other causes like radiation, vitamin supplements, drugs, cell phones usage, smoke, stress etc. are factors that are still inconclusive for causes of brain tumors.

What is important to remember of the diagnosis of these types of tumors is the fact that in more than one case the patient does not experience all the symptoms of what a person with a brain tumor should experience. Headaches could be the only predictor and therefore the patient may not see this as a dangerous symptom at the time. This could lead to the believe that some patients could have been diagnosed earlier, if it would be possible to see any lesions in the brain at that time. Sometimes the brain tumor could appear and invade dramatically over a period of only three months.

The diagnosing of the patient is quite extensive that include MRI's, CT scans, neurological tests, blood tests for cancer markers. Today the new fMRI or functional MRI may help with diagnosing the area of the brain and body that are affected by the

tumor. The location and grade of the tumor makes all the difference in treating the patient. This also will affect the patients' quality of life and day-to-day life or ADL's.

The approach of the patient and their treatment are crucial for a beneficial outcome. This will also depend on the type of tumor, benign or malignant and what stage they are in. To date only a few studies show a psychological intervention approach of the patient. The patient and the caregiver (spouse) must be informed of all the situations and treatment plans.

Including exercise in the treatment plan with cancer patients has shown a lot of positive results in the last few years. Most studies, although conducted amongst the breast cancer population, proved the influence of exercise intervention has a significant impact on the cancer patient's well-being. It is a fact that light to moderate exercises influence the brain chemistry that plays a role in neurogenesis, muscles, neurotransmission and memory and learning by enhancing the brain derived neurotrophic factor (BDNF). Due to the fact that depression plays a huge role in the affecting of the brain tumor patient's well-being, exercise will also alleviate the depression and anxiety that the patient may experience during the course of the treatment.

On the emotional side, the patients were concerned or worried about the condition or illness. Although functionality declined over time, most patients found their lives fulfilling and could cope in most cases. Some patient who found their working situation demanding showed a negative impact on their emotional, social and cognitive well-being. Having the correct support from work and home, the changes of responsibility will ease in throughout the illness and treatment. Their ADL's will change due to the lack of energy and changes in the physiology of the person itself.

In this study in most cases the patients had a lack of energy and were bothered by the side-effects of the cancer treatment. They also could not meet the needs of their family, but this is one thing that could change. The family or caregivers will become the support and take over some chores from the patient. It is a natural phenomenon that the patient

will experience insufficient energy to do everything as they previously did. The main problem of all cancer patients undergoing therapy is cancer-related fatigue that robs them from energy. Exercise has proven the fact that it could lessen the feeling of fatigue. It indicated that a third of the participants in this study did do some mild to light exercises after cancer treatment. This shows the cognitive impact during treatment. If patients are part of an exercise intervention they will adapt better to their new daily living circumstances even though it will be less responsibility than before. The fact that most of the respondents were cognitively not comfortable in some situations of the treatment they still experienced positive feedback.

The overall feeling of the respondents to participate in exercises before, during and/or after treatment shows the positive effect that exercise intervention could have on patient being diagnosed or living with a brain tumor. The incorporation of exercise intervention will be beneficial to the patient and according to the study the majority is eager to learn more about the exercise intervention show a positive attitude towards it.

The type of patients that participated in this study were close to their families, as shown in the table of social well-being. This means that most of them did have support during the stage of treatment. Fifty percent of the participants were still actively working and this could also be a supportive system to them, to help them still feel worthy and able to cope. Being positive during the process of diagnosis is very important.

Statistics also showed that the participants showed a high priority in social support to help them emotionally as well as physically in some stages of the treatment. Emotional support will improve the patient's mood in terms of depression, anxiety and worry about dying. Improving emotional well-being, will improve overall social well-being and health with regards to energy during every day life. This is why physical activity is so important. In the literature study the participants showed a positive attitude toward exercise as an adjuvant therapy alongside cancer therapy. It indicated that exercise do improve overall well-being, and in doing so also improve their QoL. Most participants will exercise at a

mild to moderate rate and at own pace. For the patient to participate in some physical activity will boost or improve brain health and overall QoL.

In this study in terms of the quality of life, patients were somewhat in control of their lives. They do get upset at some stages, but with the support that they received from their families and friends, made them handle it better. For these patients it will sooth them by saying: “ it will be okay not to be at top of things all the time.”

5.2 CONCLUSION

Due to the speculations of different therapies for brain tumor patients, no scientist or doctor can say with definite certainty that one specific treatment will be the best for all patients. A network of clinicians is part of the treatment and assorted regiments are involved in cancer therapy these days. Therefore the order in which they will be followed will be different regarding the patient’s stage and grade of the cancer or tumor. Thinking not only of the illness, but of the patients, we must regard that they may have different reactions, attitudes, and approach to cancer treatments.

The only thing that may be said with certainty is the fact that physical activity or mobility does have a way of improving the patient’s way of handling ADL’s as well as quality of life. It is unfortunately true that some patients are diagnosed in such an advanced stage that they are totally incapable to perform any physical activity. This is usually due to the high degree of radiotherapy and chemotherapy that may cause high levels of cancer-related fatigue (CRF). This exhaustion or fatigue leads to the total bedridden effect of the patient.

Although in today’s time and place, the diagnosing of brain tumors sometimes do leave space and time for a whole range of interventions that may include exercise. It is not proven as of the last couple of years, which the diagnosing of brain tumors has escalated. According to oncologists and neurologist, there is only a time frame in a year that more patients may be diagnosed with a tumor in the brain. No data or research has

shown the reason so far for this phenomenon. This does in fact not mean that diagnosing of brain tumor patients are suddenly more.

To help with early diagnosis of a brain tumor, information on symptoms is readily available on the internet, mostly information on different types of headaches that may indicate a tumor. In today's hectic living and working environment, I believe more people struggle with chronic headaches due to stress. This makes the people more aware of possible dangerous symptoms and this could help doctors or specialists to diagnose an illness or chronic disease like high blood pressure or even an invasive tumor at an early stage.

The technology also has improved in such a manner that the pinpointing of tumors is much more specific and detailed. By diagnosing the brain tumor at an early stage may influence the intervention significantly.

Diagnosing a brain tumor early on is not always the case, but there is always hope to give the patient the best possible treatment and positive feedback in terms of quality of life for the time being. No patient wants to feel that doctors and clinicians want them to sit down, give up and die. If the adjuvant therapies include sufficient psychological treatment, the patient will have a better understanding of the importance of being positive during the process of all the cancer treatment that they will receive. As going through this study, it was proven over and over again that exercise, or for this matter, light physical activity, do have a positive impact on the brain or the physical well-being of the patient. The brain is stimulated during physical activity in a lot of ways. It does not always just impact on the chemicals of the brain that "runs" the physical part of the patient, but also on a psychological manner due to the impact it has on the chemical, Serotonin. This means that the patient will benefit by improving or in the case of brain tumors, sustain the physical, as well as the psychological aspect.

Brain tumor patients will need to deal and adapt to a lot of changes as from the diagnosing stage throughout the treatment and the off treatment period. It is very

important to remember that the patient's family or spouse needs guiding as well. The adaptation to the new circumstances as well. Therefore it is very important that the family or people that will be assisting the patient also need to be informed of all the changes and procedures of the treatment.

In this study valuable information surrounding the cancer patients' way of thinking and handling of this disease with regards to exercise was demonstrated. Some aspects like marital status, employment and education have no impact on the disease, it is just an indication where and when that person is at that stage of their lives. When it comes to exercise, most patients were very positive in receiving more information on the rehabilitation in conjunction with cancer treatment. Type of exercise is mostly aerobic or daily type of activities, found in other literatures as well. Exercise was preferred to be home-based, which will mean at own pace. At own pace will lead to the understanding of moderate to more mild exercises. Regarding the preference of an exercise partner, it was either with someone close to them, but still there was a tendency of no preference of a specific person.

The frequency and time spend exercising differed before, after and while receiving cancer treatment. They would start out well, but the exercise participation became less throughout the process of cancer treatment. It can be due to the fact that the information of exercise intervention, adjuvant of cancer treatment, is not yet in place. The participants preferred to receive information by means of human contact and not via phone or internet, which is understandable. Patients in this condition want to be taken care of and feel that the informant cares about them. Therefore, it is important that therapists or the doctors that diagnose these patients or treat them know what they are doing in the psychological side of this type of cancer treatment.

Most participants in this study were motivated enough to participate in an intervention study, adjuvant to cancer treatment. This means that there is a void in this field of exercise and cancer treatment. A basis must be set to approach this illness at another level.

Through literature studies done in the forms of randomized controlled trials, pilot studies and cross sectional studies that the use of exercise intervention in cancer patients improve almost all aspects of physiological and psychological aspects of the human body even under the intervention of cancer treatment.

5.3 RECOMMENDATIONS

The holistic view and treatment of a brain tumor patient is of absolute importance. We are dealing here with a person that has cancer not the cancer that occupies the person. This is a disease that becomes “part” of the person. Therefore the patient needs to make adaptations in more ways than one. Physical-, psychological-, emotional-, social changes etc.

Information on the condition of a brain tumor is one of the most important aspects to take note of. Preparation for what to come and how to handle changes needs a lot of time. Some people that may have some type of fear avoidance may have trouble acknowledging the fact of being diagnosed with a brain tumor. This means that they will either read everything or anything on brain tumor, some facts that may not have anything to do with their situation or research absolutely nothing. It is therefore recommended that doctors (neurologists, oncologists etc.) that are part of the diagnosing team, to explain in full the situation the patient are in and what the prognosis is. Thereafter other clinical staff for example, the oncology nurse, psychologist, hospice caregivers, need to help with psychological preparation of the patient and their caregiver or spouse. This will include the stages and interval of treatments, types of medicines used, therapy session. In nowadays, it is much better to be physically and psychologically prepared for the treatment that they are about to undergo.

In this clinical team I would recommend that an Exercise specialist or Biokineticist is part of the team that will prepare and look after the patient’s physical fitness capacity. It will depends on the grade and stage of diagnosis of the brain tumor patient, and this will give the Biokineticist the indication of how to approach the patient. The exercise

intervention will in any case not be a high-level intervention, but only a low level of physical activity that the patient can handle in that certain stage of treatment. Exercise intervention for a brain tumor patient will vary from low to mild/moderate, never strenuous. It is important to note that any exercise for a cancer patient is excellent.

It is therefore recommended that a full catalogue of brain tumor treatment should be published to explain the total treatment that forms a baseline for all diagnosed brain tumors. Treatment for brain tumor patient, speaking of cancer treatments like radiation, chemotherapy, immuno-therapy and surgery are different regarding the type and grade of the tumor and therefore the exercise intervention will vary according to the type, grade and needs of that patient. Physicians that are dealing with brain tumor patients have to be fully equipped with the necessary knowledge of exercise intervention as an adjuvant therapy for them. They need to explain the consequences and benefits of exercise to them. Physicians are the first line of motivation and if they could motivate patients, it will improve the way people will look at this type of intervention in cancer therapy.

It will be beneficial to the physician to have a professional like a Biokineticist or Exercise Specialist with the necessary qualifications to refer to if they see it fit that the patient to be in this type of exercise intervention.

All of these treatments together will only help the brain tumor patient to have quality of life for longer. This is my main goal to help these types of patients to live with this disease and keep their dignity and quality of life for as long as possible.

BIBLIOGRAPHY

ADAMSEN, L., QUIST, M., ANDERSEN, C., MOLLER, T., HERRSTADT, J., KRONBORG, D., BAARDSGAARD, M.T., VISTISEN, K. MIDTGAARD, J., CHRISTIANSEN, B. STAGE, M., KRONBORG, M.T. & RORTH, M. (2009). Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomized controlled trial, *British Medical Journal*, 339 : b3410

ADLARD, P.A. & COTMAN, C.W. (2003). Voluntary exercise protects against stress-induced decreases in brain-deprived neurotrophic factor protein expression. *Neuroscience*, 124 : 985-992.

ANON. (2007). From Tryptophan to Serotonin to Melatonin: Bluemarble.com : [Online]. Available:
<http://www.home.bluemarble.net/~heartcom/tryptophantoserotonintomelatonin.html> [30 November 2010]

ANON. (2010). How exercise makes you smarter: Correct weight loss : [Online]. Available: <http://correct-weight-loss.net/2010/06/30/how-exercise-makes-you-smarter/> [1 June 2011]

ANON. (2010). Why do cancer patients need to eat healthy : [Online]. Available : www.doityourself.com/video/Why-Do-Cancer-Patients-Need-to-Eat-Healthy-and-Exercise-23-video [4 October 2011]

AMERICAN BRAIN TUMOR ASSOCIATION. (2011). Benign or malignant: What is the difference? : [Online]. Available:
<http://www.abta.org/siteFiles/SitePages/D62DBA2AF0BEEC9C9044C7CC3BA08D55.pdf> [20 May 2011]

AMERICAN BRAIN TUMOR ASSOCIATION. (2005). Edema : [Online]. Available: <http://neurosurgery.mgh.harvard.edu/abta/diction.htm> [25 September 2011].

AMERICAN CANCER SOCIETY. (2010). Sarcoma- Adult soft tissue cancer : [Online]. Available: <http://www.cancer.org/cancer/sarcoma-adultsofttissuecancer/detailedguide/sarcoma-adult-soft-tissue-cancer-soft-tissue-sarcoma>. [20 May 2011]

AMERICAN CANCER SOCIETY. (2011). Immunotherapy : [Online]. Available: <http://www.cancer.org/Treatment/TreatmentsandSideEffects/TreatmentTypes/Immunotherapy/immunotherapy.intro> [20 May 2011]

ARMSTRONG, T.S., BERGER, M.S., BONDY, M., CHANG, S., CHEW, T., CLOUGHESY, T., COBBS, C., CONN-LEVIN, N., GILBERT, M.R., GRUEN, P., GUTIN, P., MINN, Y., MOGENSEN, K., PAGE, M., PETERSON, K., PRADOS, M., RODAS, P*, ROSS, E., ROY, E., SAWAYA, R., SHAW, E., SMITH, K., SPERDUTO, P., TAMAYO, G., WALSTON, J., WEISBURG, S.M. & WRENSCH, M. (2004). The essential guide to brain tumors: Brain tumor foundation of America : [Online]. Available: <http://www.brainumor.org> [27 February 2007]

BABBIE, E. (1992). *The Practice of Social Research* (6th Ed.) California: Wadsworth Publishing Company.

BAMPOE, J., RITVO, P. & BERSTEIN, M. (1998). Quality of life in patients with brain tumor: what's relevant in our quest for therapeutic efficacy, *Neurosurgery Focus*, 3(6) : 1-10.

BARNHOLTZ-SLOAN, J.S., SLOAN, A.E. & SCHWARTZ, A.G. (1997). Relative survival rate and patterns of diagnosis analyzed by time period for individuals with primary malignant brain tumor, 1973-1997. *Journal of Neurology*, 99(3) : 458-466. [Abstract in the PUBMED database, ref. no. 12959430.]

BATTAGLINI, C.L, DENNEHY, C.A. & GROFF, D. (2006). Complementary therapies in the management of cancer treatment-related symptoms: the individualized prescriptive exercise intervention approach. *Medicina Sportiva*, 10:49–57.

BERNSTEIN, M. & BERGER, M.S. (2008). *Neuro-oncology: The Essentials*. New York, NY: Thieme Medical Publishers.

BHAGAVATHI, S & WILSON, J.D. (2009). Primary central nervous system lymphoma, *Archives of Pathology and Laboratory Medicine*, 132(11) : 1830-1934.

BROWN, J.R., HAESOOK, T.K., SHULI, L., STEPHANS, K., FISHTER, D.C., CUTLER, C., HO, V., LEE, S., MILFORD, E.L., RITZ, J., ANTIN, J.H., SOIFFER, R.J., GRIBBEN, J.G. & ALYEA, E.P. (2006). Predictors of improved progression-free survival after nonmyeloablative allogeneic stem cell transplantation for advanced chronic Lymphocytic leukemia, *Biology of Blood and Marrow transplantation*, 12(10) : 1056-1064

BROWN. D (2006). Antiepidermal growth factor receptor antibodies augment cytotoxicity of chemotherapeutic agents on squamous cell carcinoma cell lines, *Otolaryngology Head and Neck Surgery*, 122 : 75-83.

BROWN, P.D., BALLMAN, K.V., RUMMANS, T.A., MAURER, M.J., SLOAN, J.A., BOEVE, B.F., GUPTA, L., TANG-WAI, D.F., ARUSELL, R.M., CLARK, M.M. & BUCKNER, J.C. (2006). Prospective study of quality of life in adults with newly diagnosed high-grade gliomas. *Journal of Neuro-Oncology*, 76(3) : 283-291.

BONDY, M.L., EL-ZEIN, R. & WRENSCH, M. (2005). *Epidemiology of brain cancer*. In: Shiff, D. & O'Neill, B.P. (eds.), *Principles of Neuro-oncology*. New York, NY : McGraw-Hill.

CANCER COUNCIL SOUTH AUSTRALIA. (2006). Statistics Brain cancer: Cancer research SA : [Online.]. Available: <http://www.cancersa.org.au>. [18 Augustus 2011]

CANCER RESEARCH UK. (2009). Are exercise guidelines for cancer patients? : Cancer Research UK : [Online]. Available: <http://www.cancerhelp.org.uk/about-cancer/cancer-question/are-there-exercise-guidelines.html> [4 January 2011]

CANCER TREATMENT CENTERS OF AMERICA. (2008). Brain cancer treatment – Oncology rehabilitation: Cancer treatment centers of America : [Online] Available: <http://www.cancercenter.com/braincancer/physicaltherapy.cfm> [30 December 2010]

CANCER TREATMENT CENTERS OF AMERICA. (2008). Oncology rehabilitation for brain cancer: Cancer treatment centers of America : [Online]. Available: <http://www.cancercenter.com/braincancer/pt.cfm> [15 December 2010]

CELLA, D. (1998). Factors influencing quality of life in cancer patients: anemia and fatigue. *Journal of Seminars in Oncology*, 25(3 Suppl 7) : 43- 46.

CHABNER, B.A. & LONGO, D.L. (2010). Cancer chemotherapy and biotherapy: Principles and Practice. New York, NY : Lippincott Williams & Wilkins.

CHANDANA.S.R., MOVVA, S., ARORA, M. & SINGH, T. (2008). Primary brain tumors in adults, *American Family Physician*, 77(10) : 1423-1430.

CHARLES, K. (2008). Benign tumors can cause a range of problems, but their treatable by Dr. Joshua Bederson : [Online]. Available: http://articles.nydailynews.com/2008-11-19/entertainment/17911303_1_meningioma-tumor-cells. [15 April 2011]

CHEN, S., XIAO, L., LIU, Z., LIU, J & LIU, Y. (2011). Pituitary tumor transforming gene-1 haplotypes and risk of pituitary adenoma: a case-control study, *BMC Medical Genetics*, 12(44) : 2-6

CHRISTENSEN, T. & KEHLET, M.D. (1993). Postoperative fatigue, *World Journal of Surgery*, 17 : 220-225.

COMBS, S.E., THILLMAN, C., DEBUS, J. & SCHULZ-ERTNER, D. (2006). Local radiotherapeutic management of ependymomas with fractionated stereotactic radiotherapy (FSRT), *Journal of BMC Cancer*, 6(222) : 1-8.

CONN-LEVIN, N. (2005). Brain tumors and fatigue: Brain science foundation : [Online]. Available: <http://www.brainsciencefoundation.org> [14 November 2006]

COURNEYA, K.S., MACKEY, J.R. & BELL, G.J. (2003). Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes, *Journal of Clinical Oncology*, 21 : 1660-1668.

COURNEYA, K.S. (2006). Effects OF exercise and breast cancer patients and survivors: a systematic review and meta-analysis, *Canadian Medical Association Journal*, 175(1) : 34-41.

COURNEYA, K.S. (2010). Exercise for Cancer patients: Fitness after treatment. [Online]. Available: <http://www.webmd.com/cancer/features/exercise-cancer-patients.htm> [4 January 2011]

COUSSENS, L.M. & WERB, Z. (2002). Inflammation and cancer, *Nature*, 420(6917) : 860-867.

COTMAN, C.W. & BERCHTOLD, N.C. (2002). Exercise: A behavioral intervention to enhance brain health and plasticity, *TRENDS in Neurosciences*, 25(6) : 295-301.

COTMAN, C.W., BERCHTOLD, N.C. & CHRISTIE, L. (2007). Exercise builds brain health: key roles of growth factor cascades and inflammation. *TRENDS in Neuroscience*, 30(9) : 464-472.

COVALT, A. (2006). Benefits of exercise include protection from brain diseases and ageing: Huntington's disease lighthouse : [Online]. Available: <http://www.hdlighthouse.org/treatment-care/care/hdltriad/exercise.htm> [11 September 2006]

CROOKS, W., WALLER, S., SMITH, T. AND HAHN, T.J. (1991). The use of the Karnofsky performance scale in determining the outcome and risk in geriatric outpatients, *Journal of Gerontology*, 46(4) : 139-144.

DAIGNAN-FORNIER, B. & SAGOT, I. (2011). Proliferation/quiescence: the controversial "aller-retour", *Cell Division*, 6(10): 1-4.

DAVIS, J.M. & BAILEY, S.P. (1997). Possible mechanisms of central nervous system fatigue during exercise. *Journal of Medicine and Science in Sport and Exercise*, 29(1) : 45-57. [Abstract in the ScienceDirect database, ref. no. 00005768.]

DELTOUR, I., JOHANSEN, C., AUVINEN, A., FEYCHTING, M., KLAEBOE, L. & SCHUZ, J. (2009). Time trends in brain tumor incidence rates in Denmark, Finland, Norway, and Sweden, 1974-2003, *Journal of National Cancer Institute*, 101(24) : 1721-1724.

De VITA, V.T., HELLMAN, T.S. & ROSENBERG, S.A. (2008). *Cancer: Principles and practice oncology*. Philadelphia, PA : Lippincott Williams & Williams.

DEY, S., SINGH, R.H. & DEY, P.K. (1992). Exercise training: Significance of regional alterations in serotonin metabolism of rat brain in relation to antidepressant effect of exercise. *Physiology and Behavior*, 52(6) : 1095-1099.

DIMEO, F.C. (2001). Cancer related fatigue, *Cancer*, 92(6) : 1689-1693.

DIMEO, F., STIEGLITZ, R.D., NOVELLI-FISCHER, U., FETSCHER, S., MERTELSMANN, R. & KEUL, J. (1997). Correlation between physical performance and fatigue in cancer patients, *Annals of Oncology*, 8: 1251-1255.

DISCOVERY FIT & HEALTH. (2007). 5-HIAA test : [Online]. Available: <http://healthguide.howstuffworks.com/5-hiaa-dictionary.htm> [20 July 2010]

DOYLE, C., KUSHI, K.S., BYERS, T., COURNEYA, K.S., DEMARK-WAHNEFRIED, W., GRANT, B., McTIERNAN, A., ROCK, C.L., THOMPSON, C., GANSLER, T. & ANDREWS, K.S. (2008). Nutrition and Physical Activity During and After Cancer Treatment: An American Cancer Society Guide for Informed Choices, *A Cancer Journal for Clinicians*, 56 (6) : 323-352.

DURAK, E.P., HARRIS, J. AND CERIALE. (2001). The effects of exercise and quality of life improvements in cancer survivors: the results of a national survey, *Journal of Exercise Physiology online*, 4(4): 21-28.

DURMAZ, R., ERKEN, S., ARSLANTAS, A., ATASOY, M.A., BAL, C. & TEL, E. (1997). Management of Glioblastoma Multiforme: with special reference to recurrence. *Clinical Neurology and Neurosurgery*, 99 : 117-123.

eLOOK ONLINE DICTIONARY. (2011). Prognosis : [Online]. Available: <http://www.elook.org/dictionary/prognosis.html> [6 September 2011]

FREEDMAN, J. (2009). Brain cancer: Current and emerging trends in detection and treatment. New York, NY : The Rosen Publishing Group Inc.

FREIDENREICH, C.M. & COURNEYA, K.S. (1996). Exercise as rehabilitation for cancer patients, *Clinical Journal of Sport Medicine*, 6(4) : 237-244.

FRONTERA, W.R. (2006). Exercise in rehabilitation medicine (2nd ed). Champaign, IL : HumanKinetics.

GARZA, A.A., HA, T.G., GARCIA, C., CHEN, M.J. & RUSSO-NEUSTADT, A.A. (2003). Exercise, antidepressant treatment and BDNF mRNA expression in the ageing brain. *Pharmacology, Biochemistry and Behavior*, 77 : 209-220.

GERBER, L.H. (2001). Cancer rehabilitation into the future, *Cancer*, 92(4) : 975-979.

GEHRING, K., SITSKOORN, M.M., GUNDY, C.M., SIKKES, S.A.M., KLEIN, M., POSTMA, T.J., VAN DER BENT, M.J., BEUTE, G.N., ENTING, T.H., KAPPELLE, A.C., BOOGERD, W., VENINGA, T., TWIJNSTRA, A., BOERMAN, D.H., TAPHOORN, M.J.B. AND AARONSON, N.K. (2008). Cognitive rehabilitation in patients with gliomas: A randomized controlled trial, *Journal of Clinical Oncology*, 27: 3712-3722.

GILLISON, F.B., SKEVINGTON, S.M., SATO, A., STANDAGE, S. & EVANGELIDOU, S. (2009). The effects of exercise interventions on quality of life in clinical and healthy population; a meta-analysis. *Social Science and Medicine*, 68 : 1700-1710.

GOEKINT, M., ROELANDS, B., HEYMANS, E., NJEMINI, R. & MEEUSEN, R. (2011). Influence of citalopram and environmental temperature on exercise-induced changes in BDNF, *Letters in Neuroscience*, 494(2) : 150-154.

GOMÉZ-PINILLA, F. (2006). Benefits of exercise include protection from brain disease, aging : [Online]. Available: http://www.sfn.org/index.aspx?pagename=news_101706f [10 August 2009]

GREENBERG, D.B., SAWIKA, J., EISENTHAL, S. & ROSS, D. (1992). Fatigue syndrome due to localized radiation, *Journal of Pain Symptom Management*, 7 : 38-45.

GREENE, F.L. (2002). *American Joint committee: Cancer staging manual*, Philadelphia, PA : Lippincott Raven Publishers.

GUILLAMO, J., MONJOUR, A., TAILLANDIER, L., DEVAUX, B., VARLET, P., HAIE-MEDER, C., DEFER, G., MAISON, P., MAZERON, J., CORNU, P. & DELATTRE, J. (2001). Brain stem gliomas in adults: prognostic factors and classification, *Journal of Neurology*, 124(12) : 2528-2539.

HAYES, S., RYE, S., BATTISTUTTA, D., YATES, P., PYKE, C., BASHFORD, J. AND EAKIN, E. (2011). Design and implementation of the exercise and health trial – A pragmatic exercise intervention for women breast cancer, *Contemporary Clinical Trials*, 32: 577-585.

HELMENSTINE, A. (2007). Tryptophan: [Online]. Available: <http://www.chemistry.about.com> [12 September 2010]

HENSON, J.W. (2005). Glioblastoma Multiforme and Anaplastic glioma, a patient guide: Brain tumor center : [Online]. Available: <http://brain.mgh.harvard.edu/patientguide.htm> [18 September 2006]

HOBSON, K. (2008). How exercise revs up your brain: US Newshealth. [Online]. Available: <http://www.usnews.com/howexerciserevsupyourbrain.htm> [18 August 2010]

HOFFMAN, M. (2010). Exercise for cancer patients: Fitness after treatment. WebMD community.[Online].<http://www.webmd.com/cancer/features/exercise-cancer-patients.htm> [4 January 2011]

HOLLEY, S. (2000). Cancer-Related Fatigue, *Cancer Practice*, 8(2): 87-95.

HOWELL, D.C. (1992). *Statistical Methods for Psychology* (3rded.). Belmont: Duxbury Press.

INGRAM, C. & VISOVSKY, C. (2007). Exercise intervention to modify physiologic risk factors in cancer survivors. *Seminars in Oncology Nursing*, 23(4) : 275-284.

IVANHOE. (2009). Brain tumor survivors shouldn't take it easy: Medical Breakthroughs. [Online]. Available: <http://www.ivanhoe.com/channels.htm> [4 January 2011]

IVANHOE. (2009). Exercise reduces leakage through the Blood Brain Barrier: Medical Breakthroughs. [Online]. Available: <http://www.ivanhoe.com/channels.htm> [3 September 2010]

JANDA, M., STEGINGA, S., LANGBECKER, D., DUNN, J., WALKER, D. & EAKIN, E. (2007). Quality of life among patients with a brain tumor and their carers. *Journal of Psychosomatic Research*, 63(2007) : 617-623.

JEFFORD, M., MacCALLUM, P., KONG, V., MacCALLUM, P. & CHAPMAN, B. (2008). *exercise may help recovery: Cancer Council Victoria. [Online]. Available: [http://www.cancervic.org.au/about-cancer/nutrition and exercise/exercise may help recovery.html](http://www.cancervic.org.au/about-cancer/nutrition%20and%20exercise/exercise%20may%20help%20recovery.html) [4 January 2011]

JONES, L.W., GUILL, B., KEIR, S.T., CARTER, K., FRIEDMAN, H.S., BIGNER, D.D. & REARDON, D.A. (2007). Using theory of planned behavior to understand the determinants of exercise intention in patients diagnosed with primary brain cancer. *Psycho-Oncology*, 16 (2007) : 232-240.

JONES, L.W., GUILL, B., KEIR, S.T., CARTER, B.S.K., FRIEDMAN, H.S., BIGNER, D.D. AND REARDON, D.A. (2006). Patterns of exercise across the cancer trajectory in brain tumor patients, *Cancer*, 106(10) : 2224-2232.

KARIN, M. (2006). Nuclear factor-kB in cancer development and progression, *Nature*, 441: 431-436.

KO, A.H., DOLLINGER, M. & ROSENBAUM, E.H. (2002). *Everyone's guide to cancer therapy*. Kansas City, Missouri: Andrews McMeel Publishers.

KOBER, R. (2010). *Enhancing the Quality of life of people with intellectual disabilities*. New York, NY: Springer.

KONG, D. (1999). Exercise seen boosting children's brain function: National News : [Online]. Available: <http://www.dsr.wa.gov/assests/Research/Brain%20boosts> [11 September 2006]

KRAMER, A. (1970). Exercise changes brain: Huntington's Disease lighthouse.org. [Online]. Available: <http://wwwhdlighthouse.org/scripts.htm> [9 November 2006]

KRAMER, A. (2003). Journey of the developing brain: The Franklin Institute : [Online]. Available: <http://www.fi.edu/learn/exercise.html> [11 September 2006]

LAB TEST ONLINE. (2007). Lymphoma : [Online]. Available: <http://www.labtestsonline.org/understanding/conditions/lymphoma.html> [19 May 2011]

LERMAN, C., RIMER, B., BLUMBERG, B., CRISTINZIO, S., ENGSTROM, P.F., MacELWEE, N., O'CONNOR, K. & SEAY, J. (1990). Effects of coping style and relaxation on cancer chemotherapy side effects and emotional responses. *Journal of Cancer Nursing*, 13(5) : 308 – 315.

LEVIN, V.A., PHUPHANICH, S., YUNG, W.K.A., FORSYTH, P.A., DEL MAESTRO, R., PERRY, J.R., FULLER, G.N. & BAILLET, M. (2006). Randomized, double-blind, placebo-controlled trial of marimastat in Glioblastoma Multiforme patients following surgery and irradiation. *Journal of Neuro-Oncology*, 78(3) : 295-302.

LIAU, L.M. (2001). *Brain Tumor immunotherapy*. Totowa, New Jersey: Humana Press.

LICHTMAN, J.W. & SANES, J.R. (2003). Watching the neuromuscular junction, *Journal of Neurocytology*, 32(5-8) : 767-775.

LIU, R., PAGE, M., SOLHEIM, K., FOX, S. & CHANG, S.M. (2008). Quality of life in adults with brain tumors: Current knowledge and future directions, *Neuro-oncology*, 11(3) : 330-339.

LUCIA, A., EARNEST, C & PÉREZ, M. (2003). Cancer related fatigue: can exercise physiology assist oncologists? *The Lancet Oncology*, 4(10) : 616 -625.

MA, R. (2006) Types of Cancer: BC Cancer Agency : [Online]. Available: <http://www.bccancer.bc.ca/PPI/TypesofCancer/BrainnCentralNervousSystem/default.html> [6 October 2006]

MACDONALD, T. & PACKER, R.J. (2009). Pediatric medulloblastoma: Medscape : [Online]. Available: <http://emedicine.medscape.com/article/987886-overview> [1 June 2011] MARTINEZ, R., SCHACKERT, H., KIRSCH, M., PAULUS, W., JOOS, S. & SCHACKERT, G. (2005). Comparative genetic analysis of metachronous anaplastic oligoastrocytomas with extended recurrence-free interval. *Journal of Neuro-Oncology*, 72(2) : 95-102, 2005.

McARDLE, W.D., KATCH, F.I. & KATCH, V.L. (1994). *Essentials of Exercise Physiology*. Malvern, Pennsylvania : Lea & Febiger.

McNEELY, M.L, CAMPBELL, K.L., ROWE, B.H., KLASSEN, T.P., MACKEY, J.R. & COURNEYA, K.S. (2006). Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis, *Canadian Medical Association Journal*, 175 (1) : 34-41.

McQUESTION, M. (2009). Cancers of the head and neck, *Seminars of Oncology Nursing*, 25(3) : 171.

MEDALIE, M. (2009). Exercise reduces leakage through the Blood Brain Barrier: Medical Breakthroughs. [Online]. Available: <http://www.ivanhoe.com/channels.htm> [3 September 2010]

MEDICAL DICTIONARY ONLINE. (2006). Dopamine : [Online]. Available: <http://www.online-medical-dictionary.org/omd.asp?q=Dopamine> [4 January 2010]

MEDICAL DICTIONARY ONLINE. (2006). Hippocampus : [Online]. Available: <http://www.online-medical-dictionary.org/omd.asp?q=Hippocampus> [4 January 2010]

MEDIFOCUS. (2011). What is an acoustic neuroma? : [Online]. Available: <http://www.medifocus.com/2009/landinge.php?gid=TL001&?a=a&assoc=fb> [1 June 2011]

MEEUSEN, R. (2005). Exercise and the brain: insight in new therapeutic modalities, *Annals of Transplant*, 10(4) : 49-51.

MEYER, A.P. (2011). Neurologist at Netcare Unitas Hospital, Clifton Ave, Lyttelton; Centurion. Pretoria, South Africa.

MEYERS, C.A. AND HESS, K.R. (2003). Multifaceted end points in brain tumor clinical trials: cognitive deterioration precedes MRI progression, *Journal of Neuro Oncology*, 5(2):89-95, April, 30.

MOLASSIOTIS, A., WILSON, B., BRUNTON, L., CHAUDHARY, H., GATTAMANENI, R. & McBAIN, C. (2010). Symptom experience in patients with primary brain tumors: A longitudinal exploratory study. *European Journal of Oncology Nursing*, 14(5) :410-416.

MOLETE, M. (1999). National cancer registry statistics 1999: [cansa.org.za](http://www.cansa.org.za). [Online]. Available: http://www.cansa.org.za/cgi-bin/giga-cgi?cmd=cause_dir_news_item&cause_id=1056&news_id=31937&cat_id=821 [13 February 2007]

NAKAGAWA, K., AOKI, Y., FUJIMAKI, T., TAGO, M., TERAHARA, A., KARASAWA, K., SAKATA, K., SASAKI, Y., MATSUTANI, M. & AKANUMA, A. (1997). High-dose conformal radiotherapy influences the patterns of failure but did not improve survival in Glioblastoma Multiforme. *Int. Journal of Radiation Oncology*, 40(5) : 1141-1149.

NATIONAL BRAIN TUMOR SOCIETY. (2011). Brain tumors FAQ : [Online]. Available: <http://www.braintumor.org/patients-family-friends/about-brain-tumors/brain-tumor-faq.html>. [20 May 2011].

NATIONAL CANCER INSTITUTE (2006). Dictionary of cancer terms – Tumor : [Online]. Available: <http://www.cancer.gov/dictionary?cdrid=46634> [4 April 2007]

NAWA, H., CARNAHAN, J. & GALL, C. (2006). BDNF Protein Measured by a Novel Enzyme Immunoassay in Normal Brain and after Seizure: Partial Disagreement with mRNA Levels, *European Journal of Neuroscience*, 7(7): 1527-1535.

O' CONNER, T. & BROWDER, L. (1998). Development and cancer : [Online]. Available: http://people.ucalgary.ca/~browder/virtualembryo/dev_cancer.html [5 November 2011]

OLDERVOLL, L.M., KAASA, S., HJERMSTAD, M.J., LUND, J.A. & LOGE, J.H. (2003). Physical exercise results in the improved subjective well-being of a few or is effective rehabilitation for all cancer patients? *European Journal of Cancer*, 40(2003) : 951-962.

PALMIERI, D., LOCKMAN, P.R., THOMAS, F.C., HUA, E., HERRING, J., HARGRAVE, E., JOHNSON, M., FLORES, N., QIAN, Y., VEGA-VALLE, E., TASKAR, K.S.,

RUDRARAJU, V., MITTAPALLI, R.K., GAASCH, J.A., BHON, K.A., THORSHEIM, H.R., LIEWEHR, D.J., DAVIS, S., REILLY, J.F., WALKER, R., BRONDER, J.L., FEIGENBAUM, L., STEINBERG, S.M., CAMPHAUSEN, K., MELTZER, P.S., RICHON, V.M., SMITH, Q.R. & STEEG, P.S. (2009). Vorinostat inhibits brain metastatic colonization in a model of triple-negative breast cancer and induces DNA double-strand breaks, *Cancer Therapy*, 15 : 6148-6157.

PANNO, J. (2005). *Cancer: The role of genes, lifestyle and environment*. New York, NY, Facts on file inc.

PERETTI, P., BRUNEL, H., BARRIÉ, M. & CHINOT, O. (2008). Imaging in Oligodendrogliomas: Medscape : [Online] Available: <http://emedicine.medscape.com/article/342958-overview> [1 June 2011]

PETERSON, K. & WALKER, R.W. (1995). Medulloblastoma/Primitive Neuroectodermal Tumor in 45 Adults, *Journal of Neurology*, 45(3) : 440-442.

PREEDY, V.R. & WATSON, R.P. (2010). *Disease Burdens of Quality of Life Measures*, Part 4, p. 4207, New York, NY : Springer Publishers.

PURCHON, N.D. (2006). The central nervous system : [Online]. Available: <http://www.purchon.com/biology/central.htm> [12 October 2010]

RAYSON, D. & REYNO, L. (2003). Exercise and Cancer: No pain, some gain?, *Journal of Clinical Oncology*, 21(9): 1651-1652.

REAM, E., RICHARDSON, A. & ALEXANDER-DANN, C. (2006). Supportive intervention for fatigue in patients undergoing chemotherapy: A randomized controlled trial. *Journal of Pain and Symptom Management*, 31 : 148-161.

REYNOLDS, G. (2010). Phys Ed: Your brain and exercise: The New York Times : [Online]. Available: <http://well.blogs.nytimes.com/2010/07/07/your-brain-on-exercise.html> [30 November 2010]

ROBERTS, R. & MUSELLA, L. (2005). Brain tumor guide for the newly diagnosed. Virtualtrials.com : [Online]. Available: <http://www.virtualtrials.com/faq/PatientsGuide2005.pdf> [5 July 2006]

SARSILMAZ, A., GELAL, F., APAYDIN, M., VARER, M., BEZIRCIOGLU, H. & REZANKO, T. (2010). Intraventricular Glioblastoma Multiforme: A pediatric case report. *Journal of Pediatric Hematology/Oncology*, 32(6) : 519-522.

SCHNEIDER, C.M., DENNEHY, C.A. & CARTER, S.D. (2003). *Exercise and Cancer Recovery*. Champaign, IL: HumanKinetics.

SCHUBART, J.R., KINZIE, M.B. & FARACE, E. (2008). Caring for the brain tumor patient: Family caregiver burden and unmet needs. *Journal of Neuro-oncology*, 10: 61-72.

SCHWARTZ, A.L. (2003). *Cancer*. In DURSTINE, J.L. & MOORE, G.E. (eds.), *ACSM's Exercise management for persons with chronic diseases and disabilities*, United Kingdom: Human Kinetics, p. 166-172.

SCOCCIANTI, S., MAGRINI, S.M., RICARDI, U., DETTI, B., BUGLIONE, M., SOTTI, G., KRENGLI, M., MALUTA, S., PARISI, S., BERTONI, F., MANTOVANI, C., TOMBOLINI, V., DE RENZIS, C., LIOCE, M., FATIGANTE, L., FUSCO, V., MUTO, P., BERTI, F., RUBINO, G., CIPRESSI, S., FARISELLI, L., LUPATTELLI, M., SANTONI, R. & PIRTOLI, L. (2010). Patterns of care and survival in a retrospective analysis of 1059 patients with Glioblastoma Multiforme treatment between 2002 and 2007: A multicenter study by the central nervous system group of Airo (Italian Association of Radiation Oncology), *Journal of Neurosurgery*, 67(2) : 446-458.

SECER, H.I., DINC, C., ANIC, I., DUZ, B. & GONUL, E. (2008). Glioblastoma multiforme of the lateral ventricle: report of nine cases, *British Medical Journal of Neurology*, 22(3) : 398-401, 2008

SEGAL, G. (1993). Metastatic tumors to the brain and spine : De Plaines, IL : Elekta Instruments Inc.

SEGAL, R., EVANS, W. & JOHNSON, D. (2001). Structured exercise improves physical functioning in women with stage I and II breast cancer: results of randomized controlled trial, *Journal of Clinical Oncology*, 19 : 657- 665

SENERETH, E. (2002). The Biology behind “rolling”: Trends, effects and consequences of MDMA use: Serendip : [Online]. Available:
<http://www.serendip.brynmawr.edu/biology/b103/f02/web1/eserenth.html> [13 March 2007]

SEYAMA, R. & KANDA, K. (2010).The process by which families of Glioblastoma patients come through emotional pain and prepare for Hospice care. *Journal Hospice and Palliative Nursing*, 12(2) : 125-136.

SEO, T., KIM, B., KO, I., KIM, D., SHIN, M., KIM, C., YOON, J. & KIM, H. (2010). Effects of treadmill exercise on Purkinje cell loss and astrocytic reaction in the cerebellum after traumatic brain injury. *Neuroscience Letters*, 481 : 178-182.

SHELINE, G.E. (1977). Radiation therapy for brain tumors. *Cancer*, 38(1) : 873-881.

SHERR, C.J. (1996). Cancer cells, *Journal of Science*, 274(5293) :1672-1677.

SHIPP, L. & WIGGINS, M.S. (2006). Exercise benefits and cancer survivorship : [Online]. Available:

<http://www.murraystate.edu/Academics/CollegesDepartment/CollegeofHealthSciencesandHumanservices/WTS/ExerciseandCancerRecovery/Articles/Exercisebenefitsandcancersurvivorship.aspx> [4 January 2011]

SINGLETARY, S.E., ALLRED, C., ASHLEY, P. BASSETT, L.W., BERRY, D., BLAND, K.I., BORGAN, P.I., CLARK, G., EDGE, S.B., HAYES, D.F., HUGHES, L.L., HUTTER, R.V.P., MORROW, M., PAGE, D.L., RECHT, A., THERIAULT, R.L., THOR, A., WEAVER, D.L., WIEAND, H.S. AND GREENE, F.L. (2002). Revision of the American Joint Committee on cancer staging system for breast cancer, *Journal of Oncology*, 20(17): 3628-3636.

STASI, R., ABRIANI, L., BECCAGLIA, P., TERZOLI, E. & AMADORI, S. (2003). Cancer related fatigue, *Journal of Cancer*, 98(9) : 1786 – 1801.

STEEG, P., GREEN, J. & HUNTER, K. (2009). Going after the real killer: Metastatic cancer, *CCR Connections*, 3(1) : 12-17.

STRANAHAN, A.M., LEE, K., MARTIN, B., MAUDSLEY, S., GOLDEN, E., CUTLER, R.G. & MATTSON, M.P. (2009). Voluntary exercise and caloric restriction enhance Hippocampal dendritic spine density and BDNF levels in diabetic mice, *Hippocampus*, 19(10) : 951-961.

The Free *Dictionary* by Farlex (2001). Necrosis : [Online]. Available: <http://www.thefreedictionary.com/necrosis> [23 May 2011]

The Free *Dictionary* by Farlex (2001). Pinocytosis : [Online]. Available: <http://www.thefreedictionary.com/pinocytosis> [5 August 2011]

The Free *Dictionary* by Farlex (2008). Asthenia : [Online]. Available: <http://www.thefreedictionary.com/asthenia> [29 September 2011].

THOM, A. (2008). Cope with cancer: statistics : [Online]. Available: <http://www.cansa/copewithcancer/statistics.html> [30 October 2010]

TROCHIM, W.M.K. (2010). Research methods, Knowledge base : [Online]. Available: <http://www.socialresearchmethods.net/kb/statdesc.php> [9 May 2010].

VAN DER HAM, I.J.M, VAN ZANDVOORT, M.J.E., MEILINGER, T., BOSCH, S.E., KANT, N. & POSTMA, A. (2010). Spatial and temporal aspects of navigation in two neurological patients, *Journal of Cognitive Neuroscience and Neuropsychology*, 21 : 685-689.

VAYNMAN, S., YING, Z. & GOMEZ-PINILLA, F. (2004). Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition, *European Journal of Neuroscience*, 20 : 2580-2590.

VELTHUIS, M.J., AGASI-IDENBURG, S.G., AUFDENKAMPE, G. & WITTINK, H.M. (2009). The effect of physical exercise on cancer-related fatigue during cancer treatment: a meta-analysis of randomized controlled trials, *Clinical Oncology*, 22 : 208-221.

WALTERS, F.J.M. (1998). Intracranial pressure and cerebral blood flow: Update in Physiology : [Online]. Available: http://www.nda.ox.ac.uk/wfsa/html/u08/u08_013.htm [20 Augustus 2010].

WASHBURN, L. (2008). Fight cancer risk with exercise: Brain tumor support : [Online]. Available: <http://www.milesforhope.org/component/kunena/12-exercise-helps-beat-cancer.html> [4 January 2011]

WATANABE, T., KATAYAMA, Y., YOSHINO, A., FUKAYA, C. & YAMAMOTO, T. (2005). Human interferon beta, nimustine hydrochloride, and radiation therapy in the

treatment of newly diagnosed malignant astrocytomas, *Journal of Neuro-Oncology*, 72 : 57-62.

WELSH, C. (2010). Exercises for Brain Cancer patients: Livestrong.com : [Online]. Available : <http://www.livestrong.com/article/334672-exercises-for-brain-cancer-patients/#ixzz1LwtY7pzs> [21 July 2011]

Wikipedia, The Free *Encyclopedia*. (2011). Medulla : [Online]. Available: <http://en.wikipedia.org/wiki/Medulla> [14 September 2011]

Wikipedia, The Free *Encyclopedia*. (2011). Melanoma : [Online]. Available: <http://en.wikipedia.org/wiki/Melanoma> [20 May 2011].

Wikipedia, The Free *Encyclopedia*. (2011). Human Brain : [Online]. Available: http://en.wikipedia.org/wiki/Human_brain [20 September 2011].

Wikipedia, The Free *Encyclopedia*. (2011). Adjuvant therapy : [Online]. Available: http://en.wikipedia.org/wiki/Adjuvant_therapy [15 July 2011].

WIGGINS, M.S. (2004). Physical and psychosocial benefits related to exercise rehabilitation and cancer recovery: Murray State University : [Online]. Available: <http://www.murraystate.edu/Academics/CollegesDepartment/CollegeofHealthSciencesandHumanservices/WTS/ExerciseandCancerRecovery/Articles/Physicalandpsychosocialbenefitsrelatedtoexerciserehabilitationandcancerrecovery.aspx> [4 January 2011]

WILKES, G.M. & ADES, T.B. (2004). *Patient Education: Guide to Oncology Drugs*. London, UK: Jones and Bartlett Publishers.

WINDSOR, P.M., POTTER, J., McADAMS, K. & McCOWAN, C. (2009). Evaluation of a fatigue initiative: Information on exercise for patients receiving cancer treatment, *Journal of Clinical Oncology*, 21:473-482.

WINNINGHAM, M.L. (1994). Exercise and cancer. In: Goldberg, L. and ELLIOT, D.L. editors. *Exercise for prevention and treatment of illness*. Philadelphia, FA: Davis Company.

WRENSCH, M. (2008). Who gets brain tumors and why?: National Brain Tumor Foundation : [Online]. Available: <http://www.brainumor.org>. [9 September 2010]

YANG, A.V. (2006). *Trends in Brain Cancer research*. New York, NY: Nova Science Publishers.

YOUNG-McCAUGHAN, S. & ARZOLA, S.M. (2007). Exercise intervention research for patients with cancer on treatment, *Seminars in Oncology Nursing*, 23(4) : 264-274.

ZHANG, D., JOHNSTON, J.M., FOX, M.D., LEUTHARDT, E.C., GRUBB, R.L., CHICOINE, M.R., SMYTH, M.D., SNYDER, A.Z., RAICHLE, M.E. & SHIMONY, J.S. (2009). Preoperative sensorimotor mapping in brain tumor patients using spontaneous fluctuations in neuronal activity imaged with functional magnetic resonance imaging: Initial experience, *Operative Neurosurgery*, 65(1) : 226-236.

<http://www.socialresearchmethods.net/kb/statdesc.php>