

# Reports of Radiotherapy & Oncology

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# **Reports of Radiotherapy and Oncology**

**RRO**

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**ABSTRACT BOOK**

**29-31 January 2025**

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#### Editorial Office:

E-mail: rro@isro.ir/ Tel./Fax: +98-21-66567619

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- Case studies
- Critical reviews, surveys, opinions, commentaries, and essays

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## ***INTRODUCTION***

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The Ninth International Clinical Oncology Congress was held from January 29 to 31 at the Olympic Hotel in Tehran, Iran. Over the years, our goal has been to advance the scientific programs of our society and support research and development in various sectors. We strive to participate in these scientific programs, provide effective strategies, foster optimal interaction among researchers and clinicians, and offer resources to enhance scientific accountability. Additionally, we aim to create a suitable platform for informed policymaking in science and technology for youth, utilizing the facilities of organizations and scientific centers to elevate public understanding and achieve sustainable development in these fields. This year's congress focused on three main themes. The first theme was "Oncology and Personalized Medicine", which aims to tailor treatment based on each patient's unique genetic makeup, marking a new era in oncologic care. The second theme was "Use of AI in Oncology". This explored the role of artificial intelligence in transforming the landscape of oncology and cancer research. The third theme was "Ethics and Oncology", which emphasized how ethical decisions in cancer care create a framework for balancing innovation with compassion. The target audience for this congress included radiation oncologists, medical physicists, radiotherapy technicians, radiobiologists, and oncology nurses.

*Dr. Yasha Makhdomi*

*President of ISRO and ISCO Congress*

At the Ninth International Clinical Oncology Congress, we discussed the most important and recent advances in treatment options in the field of oncology. The primary goal of the congress was to enhance our understanding of oncology, which will hopefully pave the way for improving the healthcare services provided to our patients. We also saw this event as an opportunity to increase empathy and collaboration among our colleagues. Organizing this congress would not have been achievable without the assistance of the incredible people who supported us throughout the different phases of planning and implementation. We are grateful to all of these dear ones for their time and effort and value their hard work.

*Dr. Morteza Tabatabaeifar*

*Scientific Chairperson*

### ■ Therapeutic Potential of Virus-Like Particles in Breast Cancer: A Meta-Analysis of Clinical Outcomes

Maryam Kalantari Khandani <sup>1,2,\*</sup>, Masoumeh Nouri <sup>3</sup>

<sup>1</sup>Department of Radiotherapy Oncology, Shohada-e Tajrish Educational Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Surgical Oncology Research Center, Faculty of Medicine, Mashhad University of Medical Science, Mashhad, Iran

\* Corresponding Author: Dr.Maryamkalantari.khandani@gmail.com

#### Abstract

**Background:** Generally, breast cancer remains one of the leading causes of cancer-related deaths worldwide. Therefore, potent and less toxic therapeutic options are necessary for its control. Virus-like particles (VLPs) represent a modality of therapy that has emerged due to their strong immune response and delivery of targeted therapies to tumor sites. This meta-analysis aims to evaluate the therapeutic efficiency of VLP-based therapies in breast cancer, focusing on outcomes such as tumor size reduction, metastasis inhibition, and overall survival rates across different breast cancer subtypes, including HER2-positive, triple-negative, and metastatic breast cancer.

**Methods and Materials:** Data were included from 25 studies, ranging from randomized controlled trials to cohort and observational studies. The pooled effect size was estimated in a random-effects model, taking into consideration heterogeneity among studies. The main outcome measures analyzed were tumor size reduction and metastasis inhibition. Both were analyzed using correlation and regression analyses.

**Results:** There is a very strong positive relationship between tumor size reduction and metastasis inhibition, as demonstrated by a Pearson's correlation coefficient of 0.88 ( $P = 0.044$ ). Meta-regression analysis further demonstrated that tumor size reduction was significantly related to sample size ( $R^2 = 0.78$ ,  $P < 0.001$ ). Subgroup analyses revealed that HER2-negative and triple-negative breast cancer subtypes responded particularly well to VLP therapies, with average tumor size reductions of 55% and 52.5%, respectively. Sensitivity analysis was conducted to assess the robustness of the findings, and Egger's test was used to evaluate publication bias, revealing minimal asymmetry, suggesting low publication bias. Overall, the results indicate that VLP-based therapies are effective in reducing tumor size and inhibiting metastasis, particularly in more aggressive breast cancer subtypes.

**Conclusions:** These findings highlight the potential of VLPs as a targeted therapeutic approach and underscore

the need for further large-scale clinical trials to validate their long-term benefits in improving survival outcomes.

**Keywords:** Virus-like Particles (VLPs), Breast Cancer, Tumor Size Reduction, Metastasis Inhibition, Meta-analysis

### ■ Influence of P53 Expression in Clinical Outcome and Prognostic Factors in Iranian Breast Cancer Patients

Maryam Kalantari Khandani <sup>1,2,\*</sup>, Masoumeh Nouri <sup>3</sup>

<sup>1</sup>Department of Radiotherapy Oncology, Shohada-e Tajrish Educational Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Surgical Oncology Research Center, Faculty of Medicine, Mashhad University of Medical Science, Mashhad, Iran

\* Corresponding Author: Dr.Maryamkalantari.khandani@gmail.com

#### Abstract

**Background:** Breast cancer (BC) is the most common visceral cancer among Iranian women, with 13,400 new cases annually. A few studies have reported that BC patients with P53 expression have different prognoses and clinical outcomes. The aim of the present study is to evaluate and compare clinical outcomes and prognostic factors in Iranian BC patients with P53 expression.

**Methods and Materials:** In a longitudinal study, 801 BC patients who were referred to and followed by a cancer research center from 2003 to 2017 were divided into two groups of 300 patients with P53 expression (positive) and 501 patients without P53 expression (negative). Clinical outcomes and prognostic factors for these two groups were evaluated and compared.

**Results:** Patients with positive and negative P53 represented 37.5% and 62.5% of cases, with mean ages of 44.2 years ( $SD = 9.4$ ) and 47.7 years ( $SD = 10.9$ ), respectively ( $P < 0.0001$ ). There were more advanced stages and lymph node involvement, more positive lymphovascular invasion and premenopausal status, higher degrees of negative estrogen receptor (ER) status, and positive human epidermal receptor 2 (HER2) expression in patients with positive P53 compared to those with negative P53 ( $P = 0.0162$ ,  $P = 0.0047$ ,  $P = 0.0296$ ,  $P = 0.0339$ ,  $P = 0.0374$ , and  $P = 0.0494$ , respectively). In patients with positive and negative P53, five-year disease-free survival rates were 81% and 86.4% ( $P = 0.0413$ ), and five-year overall survival rates were 70% and 76.8%, respectively ( $P = 0.0323$ ).

**Conclusions:** Our study showed better clinical outcomes and favorable prognostic factors in patients without P53 expression compared with those with P53 expression.

**Keywords:** P53 Expression, Breast Cancer, Iran, Clinical Outcome

## ■ Non-randomized Phase II Trial of Concurrent Capecitabine with Brachytherapy in Treatment of Advanced Cervical Cancer Patients Eligible for Definitive Chemoradiotherapy

Soudeh Arastouei<sup>1,\*</sup>, Fatemeh Homaei Shandiz<sup>1</sup>, Sare Hosseini<sup>1</sup>, Indira Prasad Giri<sup>2</sup>, Habibollah Esmaily<sup>3</sup>, Maliheh Hasanzadeh Mofard<sup>4</sup>

<sup>1</sup>Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Purdue University Global, West Lafayette, Indiana, United States

<sup>3</sup>Faculty of Health, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>4</sup>Mashhad University of Medical Sciences, Mashhad, Iran

\* *Corresponding Author:* Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Email: Sou.arastouei@gmail.com

### Abstract

**Background:** Cervical cancer is usually diagnosed in advanced stages in developing countries due to a lack of robust screening programs. The standard treatment for advanced cervical cancer is definitive chemoradiotherapy (CRT), which consists of concurrent chemotherapy with whole pelvic external beam radiotherapy (EBRT) followed by brachytherapy (BT). The BT is not accompanied by chemotherapy, per the American Brachytherapy Society recommendation, as the high fraction size used in HDR BT could result in possible complications. This recommendation is questionable as the use of chemotherapy combined with EBRT has resulted in overall survival (OS) and progression-free survival (PFS) benefits of 12% and 16%, respectively.

**Methods and Materials:** FIGO stage IB2-IVA cervical cancer patients were screened. After external CRT, eligible patients were given capecitabine 825 mg/m<sup>2</sup> twice daily from the first until the end of their brachytherapy sessions. The primary objective of the trial was to determine the tolerability of this approach and the impact of the intervention on one-year disease-free survival (DFS) and OS rate.

**Results:** Sixty-nine patients completed treatment during the study period. Eighteen enrolled in the trial, and the other 51 patients were counted as controls. The two groups matched in terms of comorbidities, i.e., hypertension (P = 0.1) and diabetes (P = 0.42), disease stage (P = 0.14), and response to external CRT based on the pre-BT MRI study (P = 0.27). The intervention was safe, with one patient discontinuing capecitabine due to severe nausea. In one-year follow-up, two deaths occurred (one in each group), 3 patients (16.7%) recurred in the intervention group, and 10 patients (19.6%) in the control group. One-year DFS was 82% (CI: 0.54 - 0.98) in the intervention group and 87% (CI: 0.72 - 0.94) in the control group. The one-year OS rate was 93% (CI: 0.53 - 0.98) in the intervention group and 97% (CI: 0.85 - 0.99) in the control group.

**Conclusions:** Although a safe treatment approach, the addition of capecitabine to brachytherapy did not cause a statistically significant difference in one-year DFS or OS in

advanced cervical cancer. The trial was underpowered due to a low accrual rate and short follow-up.

*Keywords:* Cervical Cancer, Chemo-brachytherapy, Definitive Chemoradiotherapy, Capecitabine

## ■ Genetic Insights and Clinical Implications in the Diagnosis of Acute Myeloid Leukemia: An Updated Perspective

Nafiseh Mortazavi<sup>1</sup>, Kambiz Novin<sup>2</sup>, Aziz Eghbali<sup>3</sup>, Reza Asadpour<sup>4</sup>, Elahe Razmara Lak<sup>5\*</sup>

<sup>1</sup>Department of Pathology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Radiation Oncology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Clinical Research Development Center, Aliasghar Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Medical Parasitology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* *Corresponding Author:* Clinical Research Development Center, Aliasghar Hospital, Iran

University of Medical Sciences, Tehran, Iran. Email: Elahezazmara6@gmail.com

**Background:** Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy with diverse genetic and clinical features. The 2022 WHO classification system highlights the role of cytogenetic abnormalities in AML prognosis and therapy. This study investigates the genetic and clinical characteristics of pediatric AML to enhance diagnostic and prognostic accuracy and inform personalized treatment strategies.

**Methods:** A prospective cross-sectional study was conducted on 74 pediatric AML patients diagnosed between 2012 and 2023 at Ali-Asghar Children's Hospital, Tehran, Iran. Diagnosis was based on clinical features, hematological analysis, cytogenetic testing, immunophenotyping, and immunohistochemistry. Cytogenetic analysis utilized Giemsa banding and karyotyping, while flow cytometry assessed CD marker profiles. Nested PCR identified specific genetic rearrangements, and immunohistochemistry evaluated myeloperoxidase (MPO), lysozyme, and periodic acid-Schiff (PAS) staining. Data analysis was performed using SPSS software.

**Results:** The cohort had a mean age of 5.9 ± 5.0 years, with varying clinical features across cytogenetic subgroups. Common cytogenetic abnormalities included t(8;21), t(15;17), and t(9;11), each observed in 8 - 9 patients. Other abnormalities, such as t(1;22) and inv(16), were less frequent. Immunophenotypic analysis revealed high expression of CD34, HLA-DR, CD33, and CD45, with distinct patterns across cytogenetic groups. Patients with t(15;17) showed low CD11b and HLA-DR expression, while t(8;21) patients had altered CD34 and CD33 profiles. The study also highlighted significant variability in clinical features, including age, white blood cell count, hemoglobin, and platelet levels, with differences in symptoms like fever, fatigue, and bleeding.

**Conclusions:** The present study emphasizes the genetic and immunophenotypic diversity in pediatric AML, under-

scoring the importance of cytogenetic and molecular profiling in understanding disease mechanisms. The findings highlight the need for personalized treatment strategies based on genetic and clinical characteristics, improving risk stratification and therapeutic outcomes in pediatric AML. Further studies with larger cohorts are necessary to validate these results and identify novel therapeutic targets. **Keywords:** Acute Myeloid Leukemia, Cytogenetic Abnormalities, Prognosis, Immunophenotyping, Chromosomal Translocation

### ■ Genetic, Cytogenetic and Hematological Features in Acute Lymphoid Leukemia Patients Under Eighteen Years Old in Tehran from 2013 to 2023

Nafiseh Mortazavi <sup>1</sup>, Elahe Razmara Lak <sup>2</sup>, Aziz Eghbali <sup>2</sup>, Kambiz Novin <sup>3,\*</sup>

<sup>1</sup>Department of Pathology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Clinical Research Development Center, Aliasghar Hospital, Iran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Radiation Oncology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Radiation Oncology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran. Email: kamnar2005@yahoo.com

#### Abstract

**Background:** Acute lymphoblastic leukemia (ALL) is the most prevalent cancer in children, characterized as a hematopoietic cancer of T or B lymphoblasts. Ongoing research aims to better understand the factors contributing to ALL and create more successful treatment options. Therefore, the present study presents cytogenetic, genetic, and hematologic features from 318 ALL patients under eighteen years old.

**Materials and Methods:** The present study was a retrospective cross-sectional one. The target population included 318 children who were newly diagnosed with ALL in Tehran, Iran. All data were extracted from case files that included additional information, such as clinical data and demographic information about the patients. The flow cytometry technique was employed to perform immunophenotyping for various markers. Moreover, a standardized protocol was carried out for conventional cytogenetic analysis.

**Results:** Out of 318 patients, 179 (56.3%) were males and 139 (43.7%) were females. The most common subtype of ALL was common B cell ALL, accounting for 182 cases (57.23%), followed by Pre B Cell ALL with 74 cases (23.27%) and T Cell ALL with 27 cases (8.49%). Out of 222 patients, 17 (7.7%) had genetic abnormalities, with the highest incidence of abnormalities being associated with Runx1 (four cases). Additionally, out of 228 patients, 143 (62.7%) were identified as having cytogenetic abnormalities, with the most prevalent abnormalities being hyperdiploidy (54 cases) and t(12;21) (28 cases).

**Conclusions:** Our findings revealed the prevalence of some cytogenetic anomalies, like t(9;22) and hyperdiploidy, which are in line with what has been reported in the literature. The results of this study can provide basic information that can help guide future research on ALL patients as well as treatment options.

**Keywords:** Genetic Abnormalities, Cytogenetics, Hematologic Neoplasms, Acute Lymphoid Leukemia

### ■ Azathioprine Increases the Risk of Non-melanoma Skin Cancer Among Organ Transplant Recipients: An Update Systematic Review and Meta-analysis

Amirmohammad Salehi <sup>1</sup>, Romina Rezaei <sup>1</sup>, Salman Khazaei <sup>2</sup>, Bahareh Ebrahimi <sup>3</sup>, Alireza Sadeghi <sup>1,\*</sup>

<sup>1</sup>Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Department of Epidemiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>3</sup>Department of Dermatology, Modeling of Non-communicable Diseases Research Center, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

\* *Corresponding Author:* Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran. Email: alireza.sadeghia@gmail.com

#### Abstract

**Background and Objectives:** Non-melanoma skin cancers (NMSC), including squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), are the most common types of malignancy in organ transplant recipients (OTRs), with a steadily increasing incidence worldwide. Azathioprine (AZA) is a purine antimetabolite immunosuppressant that prevents the body from rejecting transplanted organs and is used in combination with other drugs after transplantation in OTRs. The present study aims to investigate the association between azathioprine use and the risk of NMSC among OTRs.

**Methods:** We conducted a systematic search across PubMed, Scopus, and Web of Science databases up to November 3, 2023. Eligible studies included observational studies (cohort, case-control, and cross-sectional) that reported the risk of NMSC in OTRs treated with azathioprine. The quality of the included studies was assessed using the Newcastle-Ottawa Scale checklist. Pooled risk estimates were calculated using a random-effects model. Heterogeneity was assessed via Higgins' I<sup>2</sup> and Cochrane Q statistics. Subgroup analysis was performed based on cancer type, study design, adjustment of the risk estimate, drug regimen, study quality, and organ type.

**Results:** A total of 22 studies with 19,358 patients were included in the quantitative analysis. The overall summary estimate for NMSC risk in relation to AZA treatment according to odds ratio (OR) estimates, relative risk (RR) estimates, and hazard ratio (HR) estimates were 1.79 (95% confidence interval [CI]: 1.07, 3.01), 2.09 (CI: 1.41, 3.10), and 1.12 (CI: 0.93, 1.35), respectively. There was substantial het-

erogeneity between studies in all types of OR estimates (I<sup>2</sup> = 68.94%), RR estimates (I<sup>2</sup> = 65.58%), and HR estimates (I<sup>2</sup> = 56.34%). In the subgroup analysis, there was a significant increase in SCC risk in all three estimate effects, while regarding BCC, none of them were significant. Begg and Egger tests showed no significant publication bias for OR and HR estimates.

**Conclusions:** Clinicians should be aware of the high risk of skin cancer development following solid organ transplantation. Our findings indicate that OTRs treated with AZA are at an increased risk for SCC and NMSC. Therefore, it is recommended to prioritize monitoring for skin cancer in OTRs treated with AZA.

**Keywords:** Azathioprine, Skin Neoplasms, Carcinoma, Squamous Cell, Carcinoma, Basal Cell, Transplantation

## ■ Unveiling the Prognostic Potential of Metabolic Genes in Lung Adenocarcinoma

Amirmasoud Talebian<sup>1,\*</sup>, Sobhan Ahmadvand<sup>1</sup>, Alireza Samavati<sup>1</sup>

<sup>1</sup>Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran

\* Corresponding Author: Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran. Email: Amirmasoud8081@gmail.com

### Abstract

**Background:** Lung cancer remains the foremost cause of cancer-related mortality worldwide, with lung adenocarcinoma (LUAD) being its most prevalent subtype. The metabolic reconfiguration within the tumor is vital for the initiation and progression of LUAD. Such metabolic reprogramming includes changes in pathways like glycolysis, lipid metabolism, and oxidative phosphorylation, all of which are critical for the proliferation and survival of tumors. A comprehensive understanding of the molecular dynamics of these metabolic pathways is crucial for refining prognostic assessments and formulating targeted treatments for patients with LUAD. Our study aims to clarify how metabolic gene profiles influence overall survival rates among LUAD patients. By pinpointing significant metabolic genes, we aspire to improve personalized care strategies and enhance clinical outcomes for individuals afflicted by this malignancy.

**Methods:** Gene sets associated with metabolism were obtained from the Cancer Cell Metabolism Gene Database (ccmGDB). This data supports an in-depth exploration of metabolism-related genes in various cancers. We applied Cox regression and least absolute shrinkage and selection operator (LASSO) techniques to identify the prognostic genes linked to overall survival on gene expression data retrieved from The Cancer Genome Atlas (TCGA) program. Patients were categorized into high-risk and low-risk groups based on the median value of their risk scores. Kaplan-Meier survival curves were constructed to evalu-

ate patient outcomes within these categories. The model's efficacy in differentiating between risk categories was assessed through receiver operating characteristic (ROC) curves.

**Results:** We developed a prognostic model for LUAD based on seven identified metabolic-related genes, including GSK3B, B4GALT1, PIK3CG, ACSL3, LDHA, EXT1, and HSPA1B. Cox and LASSO regression models were employed to discern these genes. Patients classified as low-risk demonstrated substantially better clinical outcomes than those identified as high-risk. ROC curve analysis validated the model's accuracy in predicting survival at one, two, and three years.

**Conclusions:** This study underscores the critical role of metabolic genes in LUAD outcomes. The prognostic model developed herein, utilizing a panel of metabolic-related genes, offers a valuable tool for precisely predicting patient survival. By delving deeper into the behavior of metabolic-associated genes, we can refine prognostic accuracy in LUAD, enabling more personalized therapeutic approaches.

**Keywords:** Lung Adenocarcinoma, Metabolic Genes, Prognosis, Overall Survival

## ■ Hub Genes that are Involved in the Resistance Mechanisms of Breast Cancer Cell Lines to Palbociclib

Mohammad Mahdi Alvandi Fard<sup>1,\*</sup>, Parisa Qayenipour<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: alvandifm4001@mums.ac.ir

### Abstract

**Background:** Breast cancer will be recognized in 12% of women. Additionally, breast cancer is the second leading cause of cancer-related mortality in women. A critical issue in the care of patients with breast cancer is treatment resistance. The goal of this study was to identify hub genes that contribute to breast cancer's resistance to treatment.

**Methods:** Microarray data of gene expression from resistant and sensitive breast cancer cell lines were downloaded from dataset GSE229002. Quality control was performed using principal component analysis (PCA) and boxplots, and differential gene expression was completed using R software. Additionally, a volcano plot and heatmap were plotted using R software. Highly expressed genes were extracted. STRING was used to create a network diagram of the identified genes. The gene network was then examined using four different methodologies, including degree, EPC, MNC, and eccentricity, with the aid of the Cytoscape plugin CytoHubba. The intersection of the four groups' preferred genes was determined by drawing a Venn diagram. Finally, the pathways involving these genes were identified through the analysis of KEGG

PATHWAY data.

**Results:** The volcano plot and heatmap showed differential gene expression between resistant and sensitive breast cancer cell lines. A network of 216 genes selected based on microarray analyses was drawn. Subsequently, the top 50 genes were discovered using each method. These four groups of genes had 16 common genes, including GRIN2D, ESR2, ERBB4, BTN3A1, IL2RB, CD8A, CACNG4, GDF15, GAPDH, DLG4, DNMT3A, GATA1, LHCGR, CD19, NTF4, and LEP. Our analysis results indicate that these genes play a critical role in some breast cancer-related pathways, such as primary immunodeficiency, PI3K-Akt signaling, mitogen-activated protein kinase (MAPK), and breast adenocarcinoma drug resistance.

**Conclusions:** The results suggest that differential gene expression between resistant and sensitive breast cancer cells can identify new genes that could be involved in resistance mechanisms and could be targeted by future studies.

**Keywords:** Breast Cancer, Drug-resistance, Differential Gene Expression, Cancer System Biology, Bioinformatics

## ■ A Systematic Review of the Recent Breakthrough in Glioblastoma Immunotherapy: Oncolytic Viruses and Emerging Future Strategies

Ali Tamimi <sup>1,\*</sup>, Seyedeh Atoosa Ramazani <sup>1</sup>

<sup>1</sup>Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran

\* Corresponding Author: Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran. Email: ali1379190@gmail.com

### Abstract

**Background:** Glioblastoma (GBM) is the most common and aggressive brain tumor. Standard treatment protocols and traditional immunotherapy are poorly effective as they do not significantly increase the long-term survival of glioblastoma patients. Oncolytic viruses (OVs) are defined as genetically engineered or naturally occurring viruses that selectively replicate in and kill cancer cells without harming normal tissues. This systematic review aims to assess oncolytic virus therapy and future perspectives of GBM immunotherapy strategies.

**Methods:** A systematic search was conducted across major medical databases (PubMed, Embase, and Cochrane Library) from 2014 to 2024. The review was based on PRISMA guidelines and utilized keywords such as “glioblastoma”, “immunotherapy”, “oncolytic viruses”, and “target therapies”.

**Results:** Out of 316 papers identified, 30 articles met the inclusion criteria. Various OVs have demonstrated efficacy against GBM in preclinical studies. Encouraging data from clinical trials have shown OVs to have a favorable safety profile and promising efficacy. For instance, in a Phase I clinical trial involving children and adolescents with recurrent or progressive high-grade gliomas, G207 demon-

strated safety and enhanced immunological response.

**Conclusions:** Oncolytic viruses have displayed promise in clinical trials, with some achieving breakthrough status. Several ongoing clinical trials are exploring the use of OVs as therapeutic agents for recurrent high-grade gliomas. While these results are promising, further clinical trials are needed to establish the safety and efficacy of OVs as a therapy for GBM. In brief, virotherapy as a standalone treatment may be effective, but combining strategies of immunotherapy and oncolytic viruses with the use of personalized approaches will pave the way toward more effective treatment regimens for GBM patients.

**Keywords:** Glioblastoma, Immunotherapy, Oncolytic Viruses, Target Therapies

## ■ Evaluation and Comparison of Radiation Dose to the Thyroid in Breast Cancer Patients Undergoing Breast and Supraclavicular Radiotherapy

Alireza Samavati <sup>1</sup>, Yasin Parvizi <sup>1,2</sup>, Shima Masumi <sup>1</sup>, Safoora Nikzad <sup>3,\*</sup>

<sup>1</sup>Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Cancer Research Center, Institute of Cancer, Avicenna Health Research Institute (AHRI), Hamadan University of Medical Sciences, Hamadan, Iran

<sup>3</sup>Department of Medical Physics, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

\* Corresponding Author: Department of Medical Physics, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran. Email: safoora2000n@yahoo.com

### Abstract

**Background:** Radiotherapy is a pivotal treatment modality for various cancers, notably breast cancer. During breast radiotherapy, the thyroid gland is incidentally exposed to the radiation field, making it essential to evaluate and compare the radiation dose received by the thyroid in patients undergoing radiotherapy for breast and supraclavicular regions.

**Methods:** A cross-sectional descriptive study was conducted on 136 breast cancer patients treated with radiotherapy at the Mahdia Center in Hamedan from 2019 to 2020. The study aimed to assess and compare the thyroid radiation dose in chest and supraclavicular radiotherapy. Data were retrieved from patients' treatment programs and thyroid contouring and analyzed using SPSS version 26 software.

**Results:** The study revealed that the average thyroid dose in chest radiotherapy was  $38.38 \pm 13.98$  cGy, while in supraclavicular radiotherapy, it was significantly higher at  $2542.78 \pm 812.95$  cGy ( $P < 0.001$ ). The thyroid V10 to V50 percentages in chest radiotherapy were zero, but in supraclavicular radiotherapy, the V10, V20, V30, V40, and V50 percentages were  $52.48 \pm 16.12$ ,  $46.15 \pm 16.38$ ,  $42.31 \pm 16.10$ ,  $38.33 \pm 16.76$ , and  $27.19 \pm 18.01$ , respectively.

**Conclusions:** Thyroid exposure to radiation during breast cancer radiotherapy is noteworthy, particularly in supraclavicular radiotherapy, where the radiation dose

exceeds permissible limits. These findings underscore the need for careful planning and protective measures to mitigate thyroid exposure during radiotherapy.

**Keywords:** Breast Cancer, Radiotherapy, Thyroid, Radiation Dose, Radiotherapy

## ■ Investigating the Combined Effects of Nanoliposomes Containing Silymarin and Radiotherapy for the Treatment of Melanoma Cancer: In Vitro Studies

Faezeh Arghidash <sup>1,2,\*</sup>, Fatemeh Gheybi <sup>1,3</sup>, Hamid Gholamhosseinian <sup>4</sup>

<sup>1</sup>Department of Medical Biotechnology and Nanotechnology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>3</sup>Nanotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>4</sup>Medical Physics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: shabnamarghidash766@gmail.com

### Abstract

**Background:** Cancer is the second leading cause of death worldwide. The main problem with chemotherapy is its side effects. Antineoplastic agents in an encapsulated form have received attention in recent years. Silymarin has multiple effects in treating cancer, and radiotherapy is a primary strategy used to control tumors. Considering the benefits provided by liposomes and the effects of radiotherapy and silymarin in cancer treatment, we decided to examine the sensitization effects of silymarin in two forms: Free silymarin (FS) and liposomal silymarin (LS), along with radiotherapy in the treatment of melanoma cancer.

**Method:** Silymarin-containing nanoliposomes were prepared by the lipid film hydration and extrusion method. The toxicity of the LS formulation compared to FS was evaluated by the MTT test. The radiosensitivity of liposomal silymarin was assessed using the colony assay. The Annexin V-FITC/PI test was used to determine the amount of apoptosis and necrosis. The ROS test was performed to measure the production of oxygen-free radicals. The expression of Bax, BCL2, P53, APAF-1, and Caspase-9 genes was evaluated by the real-time PCR method. Finally, the Caspase 3/7 activation test was used to confirm the role of LS in apoptosis induction. The cell cycle arrest assessment test was also conducted to investigate the simultaneous effects on the cell cycle.

**Results:** According to the results of the MTT test and the IC20 concentration, 20 µg/mL was selected as the treatment concentration. The colony assay showed that LS significantly increased cell death in B16F0 cells. The Annexin V-FITC/PI test and Caspase 3/7 enzyme activity indicated that increased radiation sensitivity causes increased apoptosis. The results of the cell cycle arrest indicated arrest in the G2/M phase of the cell cycle in the presence of radiation and LS. Real-time PCR results

showed that LS with radiation increases the expression of apoptosis genes and decreases the expression of the BCL-2 gene. The ROS test did not significantly increase free radical production.

**Conclusions:** Silymarin can cause radiosensitivity and a synergistic effect with radiotherapy, which is more pronounced in the liposomal form. In some cases, the observation of different results can be due to the dual effects of polyphenolic compounds.

**Keywords:** Silymarin, Radiosensitizer, Radiotherapy, Melanoma

## ■ Results of Intraoperative Radiotherapy as a Boost in Non-metastatic Breast Cancer Treated with Breast-Conserving Surgery

Elyar Mousapour Shahi <sup>1,\*</sup>, Kazem Anvari <sup>1</sup>, Fatemeh Molaei <sup>2</sup>

<sup>1</sup>Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Iran Mehr Hospital, Birjand University of Medical Sciences, Birjand, Iran

\* Corresponding Author: Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Email: elyarms@gmail.com

### Abstract

**Background:** Breast-conserving surgery combined with adjuvant radiation therapy is the most common surgical treatment for breast cancer today. Typically, radiotherapy is administered externally, covering the entire breast with an additional boost dose to the tumor bed, over a period of 6 to 7 weeks. Recently, intraoperative radiotherapy (IORT) has been employed to deliver boost doses during lumpectomy, aiming to reduce the duration of radiotherapy. This study aimed to evaluate the outcomes of IORT as a boost dose in non-metastatic breast cancer patients undergoing breast-conserving surgery.

**Methods:** This study was conducted at Omid and Imam Reza Educational hospitals and Pasteur Private Hospital, specializing in breast cancer treatment. Female patients with early-stage breast cancer (stage I-II), eligible for breast-conserving surgery with whole breast radiotherapy, were enrolled. Exclusion criteria included pregnant and lactating patients and those undergoing neoadjuvant chemotherapy. Patients underwent standard lumpectomy with a margin of at least 1 mm. During the operation, IORT was administered with a dose of 20 Gy using the ZEISS INTRABEAM 50-kV X-ray System. Subsequently, the whole breast was treated externally with a dose of 50 Gy using two tangential fields, with or without regional lymph node treatment, or a hypofractionated regimen. Patients were evaluated for treatment complications, including dermatitis, skin, and cosmetic necrosis, as well as the extent and pattern of local and systemic recurrence at two years.

**Results:** Most patients presented with T2 (45 patients, 48.4%) and N0 (51 patients, 54.8%) disease, and 70.7% (n = 65) had hormone-positive tumors. The HER2 positivity

was reported in 12 patients (13.3%). In terms of disease stage, 19 patients were stage I, 57 patients were stage II, and 11 patients were stage III. Regarding treatment toxicity, no cutaneous or subcutaneous toxicities were observed in 48 patients (55.8%). Grade 1 dermatitis was observed in 18 patients (20.9%), and grade 1 subcutaneous toxicity was reported in 30 patients (34.8%). At a median follow-up of two years, one case of locoregional recurrence in the axillary region and one case of distant recurrence were reported.

**Conclusions:** The study demonstrates that the use of IORT as a tumor bed boost dose is a safe and effective treatment approach for breast cancer patients, with acceptable side effects and low rates of severe side effects. However, long-term follow-up is necessary to determine clinical outcomes.

**Keywords:** Breast Cancer, Adjuvant Radiation Therapy, Intraoperative Radiation Therapy, Tumor Bed Boost

### ■ Evaluation of Oral Nano-silymarin Formulation Efficacy in Prevention of Diarrhea Induced by XELOX or m-FOLFOX6 Regimens in Metastatic Colorectal Cancer: A Triple Blinded, Randomized Clinical Trial

Hedyeh Karbasforooshan <sup>1</sup>, Hossein Rahimi <sup>2</sup>, Sepideh Elyasi <sup>1,\*</sup>

<sup>1</sup>Department of Clinical Pharmacy, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Department of Internal Medicine, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Department of Clinical Pharmacy, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran. Email: elyasis@mums.ac.ir

#### Abstract

**Background:** Diarrhea is a common adverse reaction associated with the FOLFOX6 and XELOX chemotherapy regimens. Silymarin, a flavonoid derived from *Silybum marianum*, has been evaluated for its potential to prevent various complications of chemotherapeutic agents, particularly through its antioxidant and anti-inflammatory properties. This study aimed to assess the efficacy of an oral nano-silymarin formulation in preventing chemotherapy-induced diarrhea in patients with metastatic colorectal cancer.

**Methods:** In this randomized, triple-blind, placebo-controlled clinical trial, 60 patients were randomly assigned to receive either 70 mg capsules containing 15% silymarin nano micelles or placebo capsules. Both were administered twice daily after meals, starting from the first day of the initial chemotherapy course and continuing through six cycles of either the XELOX or m-FOLFOX6 regimen. The severity of diarrhea was graded after the third and sixth courses of chemotherapy using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.

**Results:** The median CTCAE diarrhea scores were significantly lower in the nano-silymarin group after the third and sixth courses of chemotherapy ( $P < 0.001$ ). At both assessment points, the CTCAE score remained zero in 93.3% of patients in the treatment group, compared to only 36.7% in the placebo group. Additionally, two patients in the treatment group who experienced grade 2 diarrhea after three courses of chemotherapy saw their symptoms subside to grade 1 by the end of the sixth course.

**Conclusions:** Nano-silymarin may be considered an adjuvant medication for patients with metastatic colorectal cancer undergoing chemotherapy regimens to prevent chemotherapy-induced diarrhea. Further research with larger sample sizes is recommended for more definitive conclusions.

**Keywords:** Silymarin, Diarrhea, Colorectal Cancer, Capecitabine, 5-Fluorouracil

### ■ Hub Genes that are Involved in the Resistance Mechanisms of Glioma Cell Lines to Temozolomide

Parisa Qayenipour <sup>1,\*</sup>, Mohammad Mahdi Alvandi Fard <sup>1</sup>

<sup>1</sup>Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: Ghaenipourp4001@mums.ac.ir

#### Abstract

**Background:** Glioma is a common tumor originating in the brain. Temozolomide resistance poses a significant challenge in the management of patients with glioma. This study aimed to identify hub genes involved in the drug resistance of glioma.

**Methods:** Microarray data of gene expression from resistant and sensitive glioma cell lines (U87R) were downloaded from dataset GSE193957. Quality control was performed using principal component analysis (PCA) and boxplots, and differential gene expression analysis was conducted using R software. A heatmap was also generated using R software. Highly expressed genes were extracted, and STRING was used to construct a network of these selected genes. The gene network was analyzed using four factors: degree, EPC, MNC, and eccentricity, via the CytoHubba plugin. Survival analyses for hub genes were conducted using TCGA data.

**Results:** Quality control and heatmap plots indicated a differential gene expression pattern between the two groups. A network of 329 genes was selected based on gene expression analyses. Subsequently, the top 50 genes were identified by each method, resulting in four groups of genes with 19 common genes. Furthermore, survival analyses based on TCGA RNA-seq data demonstrated that 11 out of the 19 hub genes were significantly associated with poor prognosis in glioma cancer patients. These genes include PTPN22, ITGA5, COL1A1, HLA-DPB1, HLA-DRA, LOX, HLA-DRB1, ITGB3, ICAM1, HLA-DRB5, and IL15.

**Conclusions:** Differential gene expression between resistant and sensitive glioma cells can reveal new genes potentially involved in resistance mechanisms, which could be targeted in future studies.

**Keywords:** Glioma, Temozolomide, Brain cancer, U87R, Temozolomide resistance

## ■ Impact of Human Papillomavirus and Epstein-Barr Virus on Risk of Esophageal Cancer in Iran: A Systematic Review and Meta-analysis

Fateme Sheida <sup>1, 2, \*</sup>, Ali Mohammad Mokhtari <sup>2</sup>, Shahriar Ghodous <sup>1, 3</sup>, Amirali Soleymani Nejad <sup>1, 3</sup>, Narges Eslami <sup>1</sup>, Delaram Fadaee Heydarabadi <sup>1, 4</sup>, Ehsan Amini-Salehi <sup>1</sup>, Farahnaz Joukar <sup>1</sup>, Fariborz Mansour Ghanaei <sup>1</sup>, Soheil Hassanipour <sup>1</sup>

<sup>1</sup>Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

<sup>2</sup>Department of Epidemiology and Biostatistics, Social Development and Health Promotion Research Center, School of Health, Gonabad University of Medical Sciences, Gonabad, Iran

<sup>3</sup>Student Research Committee, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

<sup>4</sup>Student Research Committee, School of Medicine, Anzali International Campus, Guilan University of Medical Sciences, Rasht, Iran

\* *Corresponding Author:* Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran. Email: fateme.sheida1997@gmail.com

### Abstract

**Background:** Esophageal cancer (EC) is a major health concern worldwide, including in Iran. Studies suggest that viral infections, such as human papillomavirus (HPV) and Epstein-Barr virus (EBV), may contribute to EC development through oncogenic mechanisms. This study aims to investigate the potential correlation between the risk of EC and HPV/EBV in the Iranian population.

**Methods:** A systematic search was conducted within PubMed, Scopus, Embase, and Web of Science, along with Iranian databases and Google Scholar. The quality of the selected articles was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist. Comprehensive Meta-Analysis (CMA) software version 3 was used for analysis, applying event rates to estimate HPV/EBV prevalence and odds ratios (ORs) with 95% confidence intervals (CIs) to assess their impact on EC.

**Results:** Eighteen articles, including 8 cross-sectional and 10 case-control studies, were selected from 1851 records for meta-analysis. The pooled results of the meta-analysis for any type of HPV in EC patients across studies in Iran showed an event rate of 25.8% (95% CI: 19.6 - 33.2%) and an OR of 1.74 (95% CI: 0.78 - 3.85; P = 0.171). In subgroup analysis, the OR for HPV-16 and -18 was 3.44 (95% CI: 1.33 - 8.91; P = 0.011) and 2.43 (95% CI: 0.60 - 9.80; P = 0.210), respectively. The pooled event rate for EBV in EC patients was 9.8% (95% CI: 7.10 - 13.3%), and the pooled OR was 4.86 (95% CI: 1.20 - 19.61; P = 0.026).

**Conclusions:** Both HPV and EBV appear to be significant viral risk factors for EC in Iran, with HPV-16 and EBV showing the strongest associations. These findings

support the need for further research into the mechanisms of viral oncogenesis in EC and could have implications for targeted prevention strategies, such as vaccination programs.

**Keywords:** HPV, EBV, Esophageal Cancer

## ■ Health-Related Quality of Life and Cancer Related Fatigue in Patients with Non-metastatic Head and Neck Cancers

Fateme Sheida <sup>1, 2, \*</sup>, Rohollah Abbasi <sup>3, 4</sup>, Alireza Mansouri <sup>1</sup>, Zahra Keshtpour Amlashi <sup>1</sup>

<sup>1</sup>Cancer Research Center, Institute of Cancer, Avicenna Health Research Institute, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

<sup>3</sup>Department of Otolaryngology Head and Neck Surgery, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

\* *Corresponding Author:* fateme.sheida1997@gmail.com

### Abstract

**Background:** The complex nature of head and neck cancers necessitates that patients often undergo intensive multimodal treatments and face a substantial likelihood of experiencing functional and social restrictions. This study aimed to assess health-related quality of life (HRQoL) and cancer-related fatigue (CRF) in patients with non-metastatic head and neck cancers over a six-month period following treatment initiation.

**Methods:** Patients with non-metastatic head and neck cancers attending two oncology clinics in Hamadan, Iran, from April 2022 to March 2023 were evaluated. They were assessed using the brief fatigue inventory (BFI) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) version 3. Scores were recorded at baseline and six months post-treatment. All statistical analyses were performed using SPSS version 27, with a P-value of < 0.05 considered statistically significant.

**Results:** Of the 47 patients in this study, 83% were male (n = 39), and the mean age was 54.28 ± 9.61 years. The oral cavity (n = 25, 53.2%) and larynx (n = 11, 23.4%) were the most frequent tumor sites. A significant increase in CRF was observed between baseline and six months post-treatment (3.07 vs. 3.50, P < 0.001). The results of the EORTC QLQ-C30 indicated that the mean global QoL score was 73.91 ± 8.89 at baseline and decreased to 63.40 ± 9.20 six months post-treatment (P < 0.001). The majority of functional scales items reduced significantly (P < 0.001), and symptom scale items increased over time.

**Conclusions:** This study demonstrates a significant decline in quality of life (QoL) and an increase in cancer-related fatigue (CRF) among patients with non-metastatic head and neck cancers during the first six months of treatment. The findings emphasize the multifactorial impact of cancer treatments on the physical, psychological, and financial aspects of patients' lives and highlight the vital need for supportive care.

**Keywords:** Quality of Life, Cancer Related Fatigue, Head and Neck Cancer, HRQoL

## ■ The Effect of Multimedia (E-learning) in Cancer Prevention

Golnaz Zaeri <sup>1</sup>, Ali Ghanbari Motlagh <sup>2</sup>, Mahnaz Zaeri <sup>3,\*</sup>

<sup>1</sup>Department of Education and Psychology, University of Aveiro, Aveiro, Portugal

<sup>2</sup>Department of Radiation Oncology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Education and Psychology, University of Aveiro, Aveiro, Portugal

\* *Corresponding Author:* Department of Education and Psychology, University of Aveiro, Aveiro, Portugal. Email: M.zaeri66@gmail.com

### Abstract

**Background:** Cancer prevention is a critical public health priority that requires increasing public awareness and promoting health-oriented behaviors. Multimedia tools, by providing visual and interactive content, can significantly enhance cancer awareness and prevention. The present study aims to investigate the effect of multimedia tools on cancer prevention by increasing public awareness, changing health-oriented behaviors, and encouraging participation in screening programs.

**Methods:** This study was as a systematic review one. Studies were selected from reliable scientific databases and evaluated based on specific inclusion and exclusion criteria. The data were then analyzed.

**Results:** The findings indicated that multimedia tools, such as educational videos, infographics, and health applications, positively impact increasing public awareness and changing preventive behaviors. Educational videos increased awareness of risk factors by 45% through engaging visual content. Additionally, interactive programs and apps improved participation in screening programs by enabling the tracking of health-oriented behaviors.

**Conclusions:** Multimedia tools play an important role in cancer prevention due to their visual, interactive, and widely accessible capabilities. The findings demonstrate that these tools can effectively increase public awareness and strengthen preventive behaviors.

**Keywords:** Cancer, Prevention, Multimedia Education, Health-Oriented Behaviors, Public Awareness

## ■ A PEG- assisted Approach to Exosome Isolation and Doxorubicin Encapsulation: Toward Safer and Targeted Cancer Therapy

Ahlam Almanie <sup>1</sup>, Manijhe Mokhtari Dizaji <sup>1,\*</sup>, Zeinab Shankayi <sup>3</sup>, Zeinab Hormozi Moghaddam <sup>4</sup>

<sup>1</sup>Department of Medical Physics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

<sup>2</sup>Department of Medical Physics, Faculty of Medical Sciences, Baqiyatallah University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Radiology, Faculty of Allied Medical Sciences, Iran University of Medi-

cal Science, Tehran, Iran

\* *Corresponding Author:* Department of Medical Physics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran. Email: mokhtarm@modares.ac.ir

### Abstract

**Background:** Exosomes, extracellular vesicles secreted by various cell types and present in body fluids, play a crucial role in intercellular communication and biomolecular transport. Their biocompatibility and ability to cross biological barriers make them promising candidates for drug delivery, especially in cancer therapy. Doxorubicin, an effective chemotherapeutic agent, is limited by cardiotoxicity and challenges in targeting tissues, particularly in the central nervous system (CNS). This study investigates the isolation and characterization of exosomes from blood serum to evaluate their potential as carriers for doxorubicin.

**Methods:** Blood samples were collected to obtain fresh serum. Several centrifugation steps and a 0.22 µm filter were used to remove impurities. Polyethylene glycol (PEG) exosome isolation reagent was added to the filtered material. The samples were thoroughly mixed by inversion and incubated at 4°C overnight. The samples were centrifuged to pellet the exosomes, the supernatant was removed, and the exosomes were resuspended in PBS for immediate use or stored at -80°C for later use. Exosomes derived from blood serum were diluted with PBS. Doxorubicin and exosomes were thoroughly mixed and incubated at 37°C for 2 hours. The PEG reagent, previously mixed with filtered distilled water and sodium chloride and passed through a filter, was added to the exosomes and mixed for 4 hours at 4°C. Exos-Dox was obtained by centrifugation and washing with PBS. The percentage of doxorubicin encapsulation was determined by spectrophotometry at 490 nm.

**Results:** Dynamic light scattering (DLS) analysis showed that the size distribution of isolated exosomes ranged from approximately 60 nm to 289 nm, with a peak at 80 nm and a mean value of 120 nm. Flow cytometry analysis showed that the expression of CD81 and CD63, common exosome markers, was more than 70% in each sample. Transmission electron microscopy (TEM) was used to determine exosome morphology, and the exosome concentration was found to be 64.97 mg/mL by Bradford assay.

**Conclusions:** Our samples were rich in exosomes, and encapsulation efficiency was significant compared to other studies. The combination of PEG and centrifugation methods simplifies exosome isolation while maintaining efficacy. Encapsulating doxorubicin in exosomes may mitigate cardiotoxic effects and improve drug delivery across the blood-brain barrier (BBB), presenting a promising strategy for treating glioblastoma and potentially other CNS disorders.

**Keywords:** Exosomes, BBB, Polyethylene Glycol, Doxorubicin, Blood Serum

## ■ Radiotherapy in the Management of Hydatid Cyst: A Systematic Review

Fatemeh Seif<sup>1,\*</sup>, Fahimeh Fatahi<sup>1</sup>, Negar Azami<sup>2</sup>, Fatemeh Rezaeizadehgan<sup>2</sup>, Fatemeh Sadathosseini<sup>2</sup>, Zeinab Mahmoudi<sup>2</sup>

<sup>1</sup>Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran

<sup>2</sup>Student Research Committee, Arak University of Medical Sciences, Arak, Iran

\* Corresponding Author: Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran. Email: fseif@arakmu.ac.ir

### Abstract

**Background:** Hydatid cysts, the larval stage of *Echinococcus granulosus*, primarily affect organs such as the liver, lungs, brain, and bones. Standard treatments include surgery and anthelmintic medications (e.g., benzimidazole). Challenges such as accessibility and recurrence risks necessitate alternative therapies. Recent studies indicate that radiotherapy (RT) may be a promising option for curative and palliative care, although the optimal types and dosages of RT for different organs remain uncertain. The present study aims to address these gaps in knowledge.

**Methods:** A systematic review was conducted following PRISMA guidelines. Databases searched included PubMed, Embase, Scopus, and Web of Science, focusing on hydatid cysts and radiotherapy, and included studies published up to December 2024.

**Results:** From an initial pool of 226 articles, 32 studies met the inclusion criteria. A key finding was that RT at 60 Gy in 30 fractions may be effective for bone hydatid cysts.

**Conclusions:** Radiotherapy dose recommendations vary based on tissue type and the degree of cyst infiltration into adjacent organs. The RT has shown promise in treatment and palliative care. However, there are concerns about potential harm to adjacent healthy tissues, especially with 3D-RT. Advanced techniques like intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) show promise, offering enhanced precision and sparing of nearby organs at risk. The RT is ideal for inoperable cases, recurrent hydatid cysts, and treatment-resistant cases.

**Keywords:** Hydatid Cyst, Radiotherapy, Systematic Review

## ■ Radiotherapy Predictive Modeling of Secondary Cancer Risk Post-Radiation Therapy Using Machine Learning

Fatemeh Seif<sup>1,\*</sup>, Hossein Sadeghi<sup>2</sup>, Soraya Khanmohammadi<sup>2</sup>, Erfan Hatamabadi<sup>2</sup>

<sup>1</sup>Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran

<sup>2</sup>Department of Physics, Arak University, Arak, Iran

\* Corresponding Author: Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran. Email: fseif@arakmu.ac.ir

### Abstract

**Background:** The emergence of secondary cancer (SC)

as a consequence of radiation therapy (RT) represents a critical issue within the field of oncology. While RT is effective for treating primary cancers, it can sometimes result in the emergence of new, secondary malignancies. These SCs may develop months or even years after the initial treatment and are influenced by factors such as the radiation dose, the treated area, and the patient's age at the time of treatment. This study explores how advanced machine learning (ML) techniques can predict the risk of SC, utilizing a detailed dataset of patient information.

**Methods:** A range of ML algorithms, including random forests, are used to explore the intricate relationships among various factors, such as radiation dose, treatment duration, patient demographics, and genetic markers. These algorithms are selected for their capability to manage large datasets and identify complex patterns within the information. Random forests utilize an ensemble learning technique that builds multiple decision trees during the training phase and produces the most common class or the average prediction from these trees. The study's methodology encompasses several essential steps: (A) data preprocessing, (B) feature selection, (C) training and validation of models, (D) model evaluation, and (E) hyperparameter tuning.

**Results:** Key factors influencing the risk of SC are revealed through feature importance analysis, which provides insights into what contributes to the development of SC. This technique helps identify the relative significance of various variables in predicting outcomes.

**Conclusions:** The study points out the shortcomings of current predictive models, emphasizing the need to incorporate additional variables like lifestyle choices, environmental factors, and detailed genetic information. In conclusion, the study highlights the importance of broadening the range of variables included in predictive models. This expansion can lead to more accurate and personalized predictions, ultimately enhancing patient care and outcomes in oncology.

**Keywords:** Predictive Models, Secondary Cancer, Machine Learning

## ■ The Role of Topical Application of Sesame Oil in the Treatment and Prevention of Phlebitis in Patients with Colorectal Cancer Referred to Dr. Ganjavian Dezful Hospital

Mohammad Dorchin<sup>1,\*</sup>, M. B. Bigdeli Shamloo<sup>2</sup>, Mojtaba Tasbandi<sup>3</sup>, Negin Khosravani<sup>4</sup>

<sup>1</sup>Dezful University of Medical Sciences, Dezful, Iran

<sup>2</sup>Department of Nursing, Dezful University of Medical Sciences, Dezful, Iran

<sup>3</sup>Reza Radiotherapy and Oncology Specialized Center, Mashhad, Iran

<sup>4</sup>Department of Biology, Islamic Azad University of Mashhad, Mashhad, Iran

\* Corresponding Author: Dezful University of Medical Sciences, Dezful, Iran. Email: Dr.dorchin@gmail.com

### Abstract

**Background:** Cancer is one of the major health challenges. Various methods, such as chemotherapy, are primarily administered intravenously for cancer treatment. The most common complication is catheter-related phlebitis, which affects more than half of patients and poses a potential risk for infectious complications.

**Methods:** Eighty-three patients with colorectal cancer were identified according to selection criteria from June 1, 2017, to November 30, 2018, and randomly assigned to the intervention group (A) and control group (B). In group A, sesame oil, 10 drops twice a day, was applied to local phlebitis sites and then dressed. The follow-up period for patients was one week. Pain was assessed through physical examination on the first, third, fifth, and seventh days.

**Results:** The chi-square test results showed that the distribution of subjects in the two groups in terms of age, gender, location, education, marital status, occupation, race, and injection site pain was similar on the first day, with no statistically significant difference ( $P > 0.05$ ). The results of t-test indicated that pain in the third, fifth, and seventh days differed significantly between the intervention and control groups ( $P < 0.05$ ). Patients in the intervention and control groups were similar in terms of age, sex, place of residence, marital status, education, occupation, race, and site of injection. Although factors such as age and gender can affect the incidence and severity of phlebitis, the mean pain score on the third, fifth, and seventh days showed a significant difference between the intervention and control groups.

**Conclusions:** The use of local sesame oil significantly reduced the severity of pain on the third, fifth, and seventh days compared to patients who did not use topical sesame oil. Sesame oil was able to accelerate the healing and recovery process, and its topical application reduced pain caused by trauma to the body.

**Keywords:** Colorectal Cancer, Phlebitis, Sesame Oil

### ■ Neoadjuvant Chemoradiotherapy in Rectal Cancer Patients: Experience of a Single Cancer Institution in Iran

Reyhaneh Bayani <sup>1,2,\*</sup>, Nima Mousavi Darzikolaei <sup>2</sup>, Abdol-Aziz Sedighi <sup>1</sup>

<sup>1</sup>Department of Radiation Oncology, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Department of Radiation Oncology, Tehran University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Bayani.reyhane@yahoo.com

#### Abstract

**Background:** The present standard treatment for rectal cancer includes a combination of surgery, radiotherapy, and chemotherapy. Neoadjuvant chemoradiation (CRT) helps to downstage the tumor and increase the likelihood of successful surgery. The present study aimed to report the oncologic outcomes after neoadjuvant CRT in rectal cancer patients referred to a university center in the west

of Iran.

**Methods:** This retrospective cohort study was conducted on rectal cancer patients treated with long-course neoadjuvant CRT at a university hospital in Hamadan, Iran, between 2017 and 2022. Radiotherapy was administered using a 3D technique with a total dose of 50 - 50.4 Gy. Response rate, survival rate, and predictive and prognostic factors were assessed.

**Results:** Outcomes of treatment in 69 patients were analyzed. A response of any grade to neoadjuvant CRT was observed in 29 patients (42%), with 15 showing a pathologic complete response (PCR) (21.7%). There was a statistically significant association between gender ( $P = 0.01$ ), clinical overall stage, clinical T stage, clinical N stage, and pre-operative carcinoembryonic antigen (CEA) levels with treatment response. The 5-year overall survival (OS) rate was 86% among all patients. In univariate analysis, pre-operative CEA levels ( $P = 0.016$ ), older age groups ( $P = 0.028$ ), favorable pathological response ( $P = 0.03$ ), male gender ( $P = 0.023$ ), and T stage downstaging ( $P = 0.01$ ) were significantly linked to improved 5-year OS.

**Conclusions:** Our study has shown that treatment outcomes for rectal cancer patients have improved even in smaller cities. Patients now experience longer survival rates due to advancements in surgical procedures and pre- and post-operative adjuvant therapies.

**Keywords:** Neoadjuvant Chemoradiotherapy, Rectal Cancer, Rectum

### ■ Investigation of 3-Year Survival in Rectal Cancer Patients Undergoing Chemoradiotherapy or Brachytherapy with Chemoradiotherapy

Yasin Parvizi <sup>1,2,\*</sup>, Shima Masumi <sup>2</sup>, Alireza Samavati <sup>2</sup>, Abdolazim Sedighipashaki <sup>1</sup>

<sup>1</sup>Cancer Research Center, Institute of Cancer, Avicenna Health Research Institute, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup>Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran

\* Corresponding Author: yasinparvizi.bio@gmail.com

#### Abstract

**Background:** Rectal cancer is a prevalent gastrointestinal cancer and ranks as the fourth most common cancer worldwide. This study aims to compare the 3-year survival rates in rectal cancer patients undergoing chemoradiotherapy alone versus those receiving combined chemoradiotherapy and brachytherapy.

**Methods:** A retrospective cohort study was conducted involving 18 patients who received brachytherapy in addition to chemoradiotherapy (study group) and 81 patients who received chemoradiotherapy alone (control group) at the Mahdih Radiotherapy Center, Hamadan, Iran between 2005 and 2015. Patient data were extracted, compiled into a checklist, and analyzed using SPSS version 21.

**Results:** The study included 99 patients with a mean age of  $60.47 \pm 12.40$  years, comprising 62 males and 37 females. No recurrence was observed in either group. Metastasis rates in stages III, IVA, and IVB were 6.25%, 100%, and 100%, respectively ( $P < 0.001$ ). Surgical treatment resulted in the highest metastasis rate (36.36%), while primary surgery showed the lowest (0%), followed by the brachytherapy group (7.69%). The 1-, 2-, and 3-year survival rates were 94.44%, 100%, and 100% for the control group, and 96.29%, 87.5%, and 96% for the brachytherapy group.

**Conclusions:** Adding brachytherapy to chemoradiotherapy appears to reduce the frequency of metastasis and highlights the impact of disease stage on metastasis. However, there is no significant difference in the 1-, 2-, and 3-year survival rates between the two treatment groups.  
**Keywords:** Chemoradiotherapy, Brachytherapy, Rectal Cancer, Survival

### ■ Design, Implementation, and Evaluation of an Oncology Course for Medical Stager at Arak University of Medical Sciences Based on the ADDIE Model

Robab Abdi <sup>1,2,\*</sup>, Faezeh Mohseni <sup>1</sup>, Reza Nazari <sup>1</sup>, Fahimeh Fattahi <sup>1</sup>, Shiva Shabani, Azin Ahmari <sup>1,2</sup>

<sup>1</sup>Clinical Research Development Unit, Ayatollah Khansari Hospital, Arak University of Medical Sciences, Arak, Iran

<sup>2</sup>Department of Radiology, School of Medicine, Arak University of Medical Sciences, Arak, Iran. drobab61@gmail.com

\* Corresponding Author: drobab61@gmail.com

#### Abstract

**Background:** In recent decades, the prevalence of cancer has posed a serious challenge for health systems worldwide. This necessitates enhancing the clinical capabilities and oncology knowledge of medical students to provide effective care and improve the quality of life of affected patients. Given the complexities of cancer diagnosis and treatment, comprehensive and appropriate education in this field is vital. Educational courses based on theoretical and practical approaches can help strengthen the clinical skills of students.

**Methods:** An oncology training course was designed and implemented at the Ayatollah Khansari Educational Treatment Center in Arak, following the ADDIE model, which includes analysis, design, development, implementation, and evaluation. During the analysis phase, gaps in the students' knowledge and skills were identified. The course integrated both theoretical and practical training and was conducted for 20 medical interns in groups of 10 over five days, from 8 AM to 12 PM. The effectiveness of the course was evaluated using questionnaires based on the Kirkpatrick model.

**Results:** Of the 20 participating medical interns, 6 (30%) were female and 14 (70%) were male. The overall

satisfaction rate with the integrated program was 84.2%, including "very high" (31.6%) and "high" (52.6%). The mean learning of basic concepts in cancer screening significantly increased from  $2.4 \pm 0.7$  to  $3.7 \pm 0.6$  after the implementation of the educational program ( $P < 0.0001$ ). Regarding the applicability of the presented materials in the clinical setting, 89.4% chose the "agree" and "strongly agree" options. In terms of the "attractiveness" of the training course, 52.6% selected the "agree" option, and 21.1% chose the "strongly agree" option.

**Conclusions:** The evaluation results indicate positive reactions and more effective learning of clinical skills by the medical interns in the field of oncology. Based on the findings, it is necessary to incorporate an oncology internship into the general medical rotations to respond to the growing needs of healthcare systems and care standards.

**Keywords:** Oncology, Training Course and Medical Stagers

### ■ Evaluation of Tumor Clearance and Pathological Complete Response Using Induction FLOT Chemotherapy Before Neoadjuvant Chemoradiotherapy in the Treatment of Locally Advanced Adenocarcinoma of the Gastroesophageal Junction and Proximal Stomach

Zohreh Pishavar <sup>1,\*</sup>, Seyed Amir AleDavood <sup>1</sup>, Kazem Anvari <sup>1</sup>, Ehsan Soltani <sup>2</sup>

<sup>1</sup>Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Cancer Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Email: zohreh.pishavar@gmail.com

#### Abstract

**Background:** Choosing the right treatment approach for patients with adenocarcinoma of the lower end of the esophagus and the proximal part of the stomach is challenging. While the addition of chemotherapy and radiotherapy to surgery has been proven beneficial, there is no consensus on the sequence of these treatments. As the most important cause of death in this group of patients is the distant spread of the disease, earlier use of systemic treatment may be beneficial. This study aimed to investigate the benefit of induction FLOT chemotherapy prior to neoadjuvant chemoradiotherapy in the treatment of adenocarcinoma of the lower esophagus and proximal part of the stomach.

**Methodology and Materials:** In this single-arm, phase II clinical trial, patients with operable locally advanced adenocarcinoma (T1-T4b, N0-N3, M0) at the lower esophageal junction and proximal stomach in two teaching hospitals affiliated with Mashhad University of Medical Sciences [Imam Reza Hospital (Department

of Radiotherapy Oncology) and Omid Hospital] were included. Initially, patients received two courses of FLOT chemotherapy (docetaxel 50 mg/m<sup>2</sup>, oxaliplatin 85 mg/m<sup>2</sup>, leucovorin 200 mg/m<sup>2</sup>, and 5-FU 2600 mg/m<sup>2</sup> as a 24-hour infusion, all on day one, given every 2 weeks). Then, they underwent neoadjuvant chemoradiotherapy, along with a paclitaxel (50 mg/m<sup>2</sup>)/carboplatin (AUC = 2) regimen, and a total radiotherapy dose of 41.4 - 45 Gy at 1.8 - 2 Gy/day. Four to six weeks after completion of chemoradiotherapy, patients were referred for surgery. Patients were examined weekly during neoadjuvant treatments and up to one month after surgery for acute complications. The rate of acute complications, the possibility of tumor removal during surgery, and the pathological response to neoadjuvant treatment were recorded.

**Findings:** A total of 57 patients with an average age of 56.5 ± 8.3 years (range 24 - 64) were included in the study. Most lesions were T3 (23 patients, 40.4%) and N1 (26 patients, 45.6%) based on CT scan findings with and without EUS. All patients were treated with induction chemotherapy, with 51 patients (89.5%) receiving both chemotherapy courses. A total of 73.6% of patients received more than four courses of chemotherapy along with radiotherapy. Forty patients underwent surgery. Pathology results after surgery showed a complete response in 11 patients (27.5%), partial response in 10 (25%), minimal response in 12 (30%), and poor response in 7 patients (17.5%). In general, neoadjuvant treatments were tolerable in terms of hematological and gastrointestinal side effects, with most patients experiencing either zero or grade one side effects.

**Conclusions:** The results of this study demonstrate that the use of induction chemotherapy with the FLOT regimen before neoadjuvant chemoradiotherapy in patients with distal esophageal and proximal gastric adenocarcinoma is a safe and tolerable treatment approach, resulting in a complete pathological response in nearly one-third of the patients.

**Keywords:** Adenocarcinoma, Lower Part of Esophagus, Junction of Esophagus and Stomach, Proximal Part of Stomach, Sievert Classification, Neoadjuvant Chemoradiotherapy, Induction Chemotherapy

### ■ Setup Margin Evaluation for Head and Neck Radiotherapy Patients Using Electronic Portal Imaging Device

Shirin Farhang <sup>1,\*</sup>, Daryoush Khoramian <sup>1,2</sup>, Fatemeh Ranjbar <sup>1</sup>, Fatemeh Shafiei <sup>1</sup>, Sepideh Saadatmand <sup>1</sup>, Fatemeh Zahedi <sup>1</sup>

<sup>1</sup>Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran

<sup>2</sup>Department of Medical Physics, The Advocate Center for Clinical Research, Ayatollah Yasrebi Hospital, Kashan, Iran

\* Corresponding Author: Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran. Email: shirin\_farhang@ymail.com

#### Abstract

**Background:** This study aims to determine the magnitude of systematic and random errors during patient setup for head and neck cancer patients to provide setup margin (SM) errors. The SM is the margin that should be added to account for uncertainties during the radiotherapy treatment course.

**Methods and Materials:** Clinical target volume (CTV) to planning target volume (PTV) margin errors (setup margin-SM) were calculated according to the formula presented by the International Commission on Radiation Units and Measurements (ICRU) report no. 62, Stroom and Heijmen, and Van Herk et al. A total of 470 images (23 patients) were acquired in anterior–posterior (AP), medio-lateral (ML), and superior–inferior (SI) directions using an on-board electronic portal imaging device (EPID). All measurements were performed on an Elekta Synergy Linac. Before conducting the research, the alignment of the EPID and the machine isocenter was checked.

**Results:** Calculated population systematic errors were 1.4 mm, 1.2 mm, and 1.7 mm in the AP, ML, and SI directions, respectively. Calculated population random errors were 1.4 mm, 1.8 mm, and 2.2 mm in the AP, ML, and SI directions, respectively. The calculated SM according to ICRU 62 were 2 mm, 2.2 mm, and 2.9 mm in the AP, ML, and SI directions, respectively. The calculated SM according to Stroom and Heijmen were 3.8 mm, 3.7 mm, and 5 mm in the AP, ML, and SI directions, respectively. The calculated SM according to Van Herk et al. were 4.7 mm, 4.4 mm, and 6 mm in the AP, ML, and SI directions, respectively.

**Conclusions:** Evaluating the SM is crucial for every radiotherapy center to ensure the prescribed dose is delivered to the target volume. By averaging the SM for each direction, we determined setup margins of 3.5 mm, 3.4 mm, and 4.6 mm in the AP, ML, and SI directions, respectively.

**Keywords:** Setup Margin, Head and Neck, Radiotherapy

### ■ Mitigating Radiation-Induced Hypothyroidism in Head and Neck Oncology: Screening, Treatment, and Advanced Imaging Techniques

Azin Ahmari <sup>1,2</sup>, Fahimeh Fattahi <sup>1,\*</sup>, Fatemeh Seif <sup>1,2</sup>, Robab Abdi <sup>1,2</sup>

<sup>1</sup>Clinical Research Development Unit, Ayatollah Khansari Hospital, Arak University of Medical Sciences, Arak, Iran

<sup>2</sup>Department of Radiology, School of Medicine, Arak University of Medical Sciences, Arak, Iran

\* Corresponding Author: Clinical Research Development Unit, Ayatollah Khansari Hospital, Arak University of Medical Sciences, Arak, Iran. Email: Ffattahi1@gmail.com

#### Abstract

**Background:** Radiation therapy is a cornerstone in the treatment of head and neck cancers, providing substantial benefits in tumor control. However, a significant complication from neck irradiation is radiation-induced hypothyroidism (RIHT). This condition can manifest as subclinical or clinical hypothyroidism, leading to serious

health risks, including metabolic dysregulation and cardiovascular issues. The relationship between radiation dose and the development of hypothyroidism is complex, highlighting the need for vigilant monitoring of thyroid function in patients undergoing neck radiotherapy.

**Methods:** The first question is when to start and how long to continue screening for hypothyroidism after thyroid irradiation. According to surveys, different levels of thyroid dysfunction can occur a few months after finishing irradiation, ranging from less than three months to one year. Current guidelines recommend screening for thyroid dysfunction using TSH and free T4 tests after the initial follow-up visit, with ongoing monitoring throughout a patient's life. When hypothyroidism is diagnosed, immediate initiation of hormone replacement therapy with levothyroxine is vital for symptom relief and normalization of thyroid hormone levels. Conservative starting doses — ranging from 12.5 to 50 mcg per day — are advised, particularly for older patients or those with cardiovascular conditions, with TSH levels monitored within 4 to 12 weeks post-initiation.

**Results:** Research shows that radiation doses exceeding 30 Gy significantly increase the risk of developing hypothyroidism. Different radiation therapy techniques — such as 3D conformal radiotherapy (3D CRT), intensity-modulated radiotherapy (IMRT), and volumetric modulated arc therapy (VMAT) — vary in their impact on thyroid exposure. The 3D CRT generally exposes the thyroid to a greater volume of radiation, while IMRT and VMAT can be adjusted to spare healthy tissues, potentially lowering the risk of hypothyroidism. Key dosimetric parameters include the mean dose to the thyroid (Dmean) and volume thresholds (such as V30 and V50), which are critical predictors of post-radiotherapy hypothyroidism risk.

**Conclusions:** A comprehensive strategy incorporating diligent screening, advanced imaging, and personalized radiation treatment is vital for improving head and neck oncology outcomes and enhancing the quality of life for affected patients. Advanced imaging techniques, such as magnetic resonance imaging (MRI) and FDG-PET CT, also play an essential role in optimizing treatment planning and improving the delineation of target volumes while minimizing unnecessary radiation exposure. Continued research is essential to further mitigate risks associated with RIHT.

**Keywords:** Radiation Therapy, Thyroid Gland, Head and Neck Cancers

## ■ Assessment of Critical Organs Integral Dose in Prostate Radiation Therapy with 3D-CRT and IMRT Methods Using Monte Carlo

Fatemeh Shafiei<sup>1</sup>, Fatemeh Ranjbar<sup>1</sup>, Saeed Karimkhani Zandi, Mohammad Abbasiyan Motlaq, Daryoush Khoramian<sup>1,2</sup>, Soheil Elmtalab, Sepideh Saadatmand<sup>1,\*</sup>

<sup>1</sup>Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran

<sup>2</sup>Department of Medical Physics, The Advocate Center for Clinical Research, Ayatollah Yasrebi Hospital, Kashan, Iran

\* Corresponding Author: Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran. Email: saadatmandsepideh198@gmail.com

### Abstract

**Background:** The present study aims to evaluate and compare the integral dose to organs at risk (OARs) and the planned target volume (PTV) using two radiotherapy techniques: 3D-CRT (18 MV) and IMRT (6 MV). Simulations were performed using the GATE Monte Carlo code.

**Methods and Materials:** Plans for thirty male prostate cancer patients undergoing radiotherapy with 3D-CRT (18 MV) and IMRT (6 MV) techniques were investigated. The 3D-CRT plans consisted of four irradiation fields in the first phase and seven fields in the second phase, while the IMRT plans involved nine irradiation fields. Following the delineation of the target volume (prostate and lymph nodes) and OARs (rectum, bladder, left and right femoral heads, and small bowel) according to RTOG criteria, treatment plans were designed using the MONACO treatment planning system (version 5.11.03, UK). The prescribed dose, approved by an oncologist, was 78 Gy (2 Gy per fraction). The linear accelerator head (Elekta Synergy) was modeled using the GATE Monte Carlo code (version 7) and validated through percentage depth dose and dose profile. Treatment simulations for each patient were conducted under clinical irradiation conditions, including the number, size, angles of irradiation fields, and MLC configurations. The integral doses to the PTV and OARs were then estimated using a voxelized phantom.

**Results:** The mean integral dose in the 3D-CRT technique, based on GATE simulations, to the PTV was estimated as  $75.65 \pm 4.96$  Gy. The dose for OARs was calculated as  $75.65 \pm 4.96$  Gy for the rectum,  $59.45 \pm 5.60$  Gy for the bladder,  $60.07 \pm 4.66$  Gy for the left femoral head,  $46.38 \pm 3.43$  Gy for the right femoral head, and  $35.06 \pm 11.18$  Gy for the small bowel. In contrast, for the IMRT technique, the mean integral dose to the PTV was observed as  $79.46 \pm 0.38$  Gy. The dose for OARs was calculated as  $56.88 \pm 3.51$  Gy for the rectum,  $35.06 \pm 11.18$  Gy for the bladder,  $52.82 \pm 3.99$  Gy for the left femoral head,  $50.03 \pm 4.94$  Gy for the right femoral head, and  $32.02 \pm 6.66$  Gy for the small bowel. The relative difference percentage (RD%) in integral dose between the two techniques for the PTV was -5.0363%, while for the OARs, it was calculated as 11.1522% for the rectum, 16.7138% for the bladder, 36.5028% for the right femoral head, 50.7559% for the left femoral head, and 5.8185% for the small bowel.

**Conclusions:** The IMRT technique delivered higher integral doses to the PTV while reducing the integral dose to surrounding OARs compared to the 3D-CRT technique. These differences were statistically significant ( $P < 0.05$ ), favoring IMRT for better dose distribution and reduced risk to adjacent organs.

**Keywords:** IMRT, Organ at Risk, Integral Dose, Monte Carlo

## ■ Evaluation of Organs at Risk Integral Dose in Left Breast Radiation Therapy 3D-CRT and IMRT Using Monte Carlo Simulation Code

Fatemeh Ranjbar<sup>1</sup>, Fatemeh Shafiei<sup>1</sup>, Fatemeh Zahedi<sup>1</sup>, Mohammad Abbasiyan Motlaq, Hamideh Naderi, Sepideh Saadatmand<sup>1\*</sup>

<sup>1</sup>Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran

\* Corresponding Author: Department of Medical Physics, Teb Parto Sadra Radiotherapy Center, Qom, Iran. Email: saadatmandsepideh198@gmail.com

### Abstract

**Background:** The present study aims to evaluate and compare the integral dose to organs at risk (OARs) and the planned target volume (PTV) using two radiotherapy techniques: Three dimensional conformal radiotherapy (3D-CRT) with 6 MV and 18 MV, and intensity-modulated radiotherapy (IMRT), through simulations performed with the GATE Monte Carlo code.

**Methods:** The study investigated radiotherapy plans for thirty female patients with left breast cancer using 3D-CRT (6 MV and 18 MV) and IMRT (6 MV) techniques. The 3D-CRT plans included two tangential radiation fields (medial and lateral) and supraclavicular fields [anterior-posterior/posterior-anterior (AP/PA)], while the IMRT plans involved seven irradiation fields. Target volumes, including the left breast, lymph nodes, and OARs (heart, left lung, and contralateral right breast), were contoured according to RTOG criteria. Treatment plans were created using the MONACO treatment planning system (version 5.11.03, UK). The prescribed dose, approved by an oncologist, was 50 Gy (2 Gy per fraction). The linear accelerator head (Elekta Synergy) was modeled using GATE (version 7) and validated through percentage depth dose and dose profile. Treatment simulations for each patient were conducted under clinical conditions, including parameters such as the number, size, and angles of irradiation fields and MLC configurations. The integral dose to the target and OARs was estimated using a voxelized phantom.

**Results:** The mean integral dose obtained from simulation using the GATE code in the 3D-CRT treatment technique for the PTV and OARs, including the heart, left lung, and right breast, was estimated as 50.64 ± 3.80 Gy, 17.34 ± 3.61 Gy, 26.4 ± 5.40 Gy, and 5.6 ± 2.64 Gy, respectively. In the IMRT treatment technique, the integral mean dose for the PTV and OARs, including the heart, left lung, and right breast, was calculated as 53.60 ± 2.29 Gy, 11.22 ± 2.58 Gy, 14.6 ± 2.80 Gy, and 2.71 ± 3.81 Gy, respectively. The relative difference percentage (R.D.%) integral dose between the two techniques, 3D-CRT and IMRT, for the PTV and OARs, including the heart, left lung, and right breast, was observed as -5.8452%, 35.2941%, 44.6970%, and 51.6071%, respectively.

**Conclusions:** The mean integral dose to OARs was higher in the 3D-CRT technique compared to IMRT. However, the IMRT technique significantly reduced the dose to OARs

while effectively targeting the tumor. Additionally, the mean integral dose to the PTV was higher in the IMRT technique than in 3D-CRT ( $P < 0.05$ ).

**Keywords:** Integral Dose, Organ at Risk, 3DCRT, IMRT

## ■ Artificial Intelligence in Radiotherapy Treatment Planning: Current Applications, Challenges, and Future Directions

Fatemeh Zahra Nosrati<sup>1\*</sup>, Ali Shabestani Monfared<sup>2</sup>

<sup>1</sup>Babol University of Medical Sciences, Babol, Iran

<sup>2</sup>Cancer Research Center, Health Research Institute, Babol University of Medical Science, Babol, Iran

\* Corresponding Author: Babol University of Medical Sciences, Babol, Iran. Email: f.nosrati1221@gmail.com

### Abstract

**Background:** Artificial intelligence (AI) is transforming radiotherapy treatment planning, offering unprecedented opportunities for personalization, efficiency, and precision in cancer care. The present review study provides a comprehensive overview of AI's current applications, challenges, and future directions in radiotherapy treatment planning.

**Methods and Materials:** Current applications of AI in radiotherapy include automatic segmentation, automated treatment planning, online adaptive radiotherapy, and decision-making for personalized treatment selection. Deep learning techniques, particularly convolutional neural networks, have emerged as powerful tools for various tasks in the radiotherapy workflow. Successful implementations have been reported in imaging analysis, dose prediction, and quality assurance processes. However, challenges persist in implementing AI in radiotherapy, including data privacy concerns, reliability and interpretability of AI models, regulatory considerations, and interobserver variability in contouring. Ethical issues related to AI-generated data ownership, bias in training datasets, and redefining clinical trials for AI evaluation remain unresolved.

**Results:** Future directions include ongoing research in AI-enhanced online adaptive radiotherapy, motion tracking, and predictive modeling for personalized treatment planning. Emerging technologies such as MR-linacs and advanced machine learning algorithms promise to revolutionize radiotherapy workflows. As AI continues to integrate into clinical practice, addressing ethical, legal, and quality control aspects is crucial to ensure responsible implementation.

**Conclusions:** This review study aims to provide a comprehensive overview of the current state-of-the-art AI applications for radiotherapy treatment planning, highlighting both the promising advancements and the remaining challenges in this rapidly evolving field.

**Keywords:** Artificial Intelligence, Radiotherapy Planning, AI

## ■ The Evolving Role of Radiation Therapists in Modern Oncology: Balancing Technology and Patient Care

Soroush Najafi Sarvestani <sup>1,2,\*</sup>, Mohammad Javad Enferadi Aliabad <sup>2</sup>, Abolfazl Kanani <sup>1</sup>

<sup>1</sup>Pardis Cancer Research Center, Pardis Cancer Institute, Shiraz, Iran

<sup>2</sup>Department of Medical Physics, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

\* Corresponding Author: sorooshnajafi@gmail.com

### Abstract

**Background:** Radiation therapy (RT) is at the forefront of cancer treatment, utilizing advanced tools to target tumors with precision while safeguarding healthy tissues. Radiation therapists (RTTs) are more than just technicians — they are critical team members who bridge technology and patient care. This study explores the evolving responsibilities of RTTs, emphasizing their growing impact on precision treatment, safety, and patient support.

**Materials and Methods:** Understanding the change: This study reviewed how advancements such as MR-guided radiation therapy and adaptive radiation therapy (ART) are reshaping RTT roles. It explored updated clinical guidelines that demand more active RTT involvement and assessed the impact of RTTs on treatment quality, using examples like daily imaging and quality assurance (QA).

**Key contributions:** The study highlights the role of RTTs in adapting treatment plans to individual patient needs through ART, their involvement in identifying and correcting setup errors in real time using cone-beam computed tomography (CBCT), and their leadership in daily QA to ensure equipment and treatment precision meet safety standards.

**Results:** How RTTs make a difference: Sharper focus on precision: The RTTs achieve alignment accuracies within 2 mm, particularly in advanced techniques like intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). They use CBCT to minimize setup errors and adjust treatments for even the most complex cases.

**Stepping up in QA:** The RTTs ensure radiation doses remain within  $\pm 3\%$  of prescribed levels. Advanced practice RTTs (APRTs) develop tailored imaging protocols and independently manage safety metrics.

**Active problem solvers:** The RTTs identify potential issues during treatments and act quickly to correct them, ensuring optimal patient outcomes.

**Better outcomes for patients:** The involvement of RTTs leads to reduced errors and improved safety in treatment delivery. They provide greater emotional and physical support for patients, offering a reassuring presence during challenging times.

**Conclusions:** Radiation therapists are redefining their roles, moving beyond traditional tasks to become leaders in treatment precision, safety, and patient care. As technology evolves, so too must RTTs, embracing ongoing ed-

ucation and new responsibilities. Their expertise ensures not only technical excellence but also a human touch that makes all the difference for patients navigating cancer treatment.

**Keywords:** Radiation Therapists, RTT, Modern Oncology

## ■ Revolutionizing Personalized Breast Cancer Treatment: A Systematic Review of AI's Advancements and Challenges

Amirhosein Vatandoost <sup>1</sup>, Mozafar Naserpour <sup>2</sup>, Sahel Heydarheydari <sup>2,\*</sup>

<sup>1</sup>Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* Corresponding Author: Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: Sheydari7@gmail.com

**Background:** Patients with breast cancer exhibit distinct microbiological profiles and varying reactions to treatments despite having the same disease. Personalized treatment approaches for breast cancer emphasize the customization of therapeutic regimens based on the unique biological and clinical characteristics of each patient, including the histological type of cancer, disease stage, and relevant health history. Artificial intelligence (AI) is increasingly crucial in enhancing breast cancer treatment plans by utilizing comprehensive datasets, including genomic data, clinical trial findings, and patient outcomes. This systematic review evaluates recent advancements and challenges in using AI for personalized breast cancer treatment, emphasizing its influence on clinical decision-making and patient outcomes.

**Methods:** A systematic literature search was conducted without time restriction, using databases such as Scopus, PubMed, and Web of Science. Citation tracking tools such as PubMed and Google Scholar were also utilized to ensure a comprehensive search. The inclusion criteria were limited to original, peer-reviewed studies published in English. The quality of the selected articles and the risk of bias were assessed following the PRISMA 2020 guidelines.

**Results:** The findings highlight the transformative impact of AI in advancing breast cancer care. Deep learning models have demonstrated significant accuracy in predicting treatment responses and patient prognosis. Additionally, neural networks and transfer learning techniques have enhanced the precision of survival predictions and improved the classification of tumor subtypes. Machine learning approaches have consistently demonstrated high accuracy, often exceeding 90% in cancer detection. These methods have also shown potential in reducing false positives by approximately 30%. Despite advancements, challenges persist, including limited high-quality datasets, integration barriers in clinical workflows, and ethical concerns such as data privacy, transparency, and equitable access.

**Conclusions:** The present review study highlights the role of AI in improving breast cancer management by an-

alyzing complex datasets, predicting treatment efficacy, and aiding oncologists in personalized decision-making. However, addressing challenges related to data diversity, system validation, and ethical concerns is critical to optimizing AI's role in clinical practice.

**Keywords:** Breast Cancer, Artificial Intelligence, Personalized Treatment, Clinical Decision-Making

## ■ High-Frequency Image-Guided Radiation Therapy in Stage III Non-Small-Cell Lung Cancer: A Systematic Review of Outcomes

Amirhosein Vatandoost<sup>1</sup>, Sahel Heydarheydari<sup>2,\*</sup>

<sup>1</sup>Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

\* *Corresponding Author:* Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: sheydari7@gmail.com

### Abstract

**Background and Objectives:** High-frequency image-guided radiotherapy (hfIGRT) is increasingly adopted for managing stage III non-small-cell lung cancer (NSCLC), but its clinical advantages remain underexplored. While previous studies focused on dosimetry and secondary cancer risks linked to imaging techniques such as electronic portal imaging devices (EPID) and cone beam computed tomography (CBCT) in stereotactic body radiation therapy (SBRT), recent advancements such as ultrafast kV-MV-CBCT during 15-second breath-holds offer improved imaging speed, patient comfort, and reduced radiation exposure. This study aims to review the outcomes of hfIGRT in stage III NSCLC, with a specific focus on the feasibility and clinical implications of excluding clinical target volumes (CTV) while maintaining treatment efficacy.

**Methods:** A systematic literature search was conducted without time restriction, using databases such as Scopus, PubMed, and Web of Science. Citation tracking tools such as PubMed and Google Scholar were utilized to ensure a comprehensive search. The inclusion criteria were limited to original, peer-reviewed studies published in English. The quality of the selected articles and the risk of bias were assessed following the PRISMA 2020 guidelines.

**Results:** High-frequency IGRT has advanced treatment precision but has not significantly improved survival metrics, with a median overall survival of approximately 22 months and a two-year locoregional control rate of 69%. Imaging doses from MV-EPID increased secondary cancer risk by more than 8.5 times compared to kV-CBCT, highlighting the significantly lower risk associated with kV-CBCT. Ultrafast kV-MV-CBCT minimized imaging time to 15 seconds, reducing healthy tissue exposure by 30% and achieving submillimeter setup accuracy (mean error ~ 0.5 mm). Residual setup errors, especially toward the

heart, negatively impacted survival (hazard ratio ~ 1.1), emphasizing the importance of strict protocols. Omitting CTV showed high efficacy, with a failure-free survival rate of 98% over two years.

**Conclusions:** High-frequency IGRT improves precision in stage III NSCLC treatment but has limited survival benefits and increased costs. MV-EPID poses higher secondary cancer risks than kV-CBCT, while ultrafast kV-MV-CBCT reduces imaging time, spares healthy tissue, and allows for safe CTV omission. Stricter protocols are needed to protect dose-sensitive organs, with further research required to optimize safety, efficacy, and cost.

**Keywords:** High-Frequency Image-Guided Radiation Therapy (hfIGRT), Non-Small-Cell Lung Cancer (NSCLC), Stereotactic Body Radiation Therapy (SBRT)

## ■ Evaluating the Improvement of Radiation Treatment Planning for Patients with Glioblastoma Multiform Tumor by Using the Fusion of Images Obtained from Magnetic Resonance Imaging and Computed Tomography and Dosimetry of the Eye Area

Sasan Tizro<sup>1,2,\*</sup>, Ali Shabestani Monfared<sup>3</sup>, Danial Fazilat Panah<sup>3</sup>, Fatemeh Zahra Nosrati<sup>1</sup>, Davoud Jahansouz<sup>4</sup>

<sup>1</sup>Department of Medical Physics, Babol University of Medical Sciences, Babol, Iran

<sup>2</sup>Radiology Center, Salamat Hospital, Guilan University of Medical Science, Guilan, Iran

<sup>3</sup>Cancer Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

<sup>4</sup>Non-communicable Disease Institute, Mazandaran University of Medical Science, Mazandaran, Iran

\* *Corresponding Author:* yahill2013@gmail.com

### Abstract

**Background:** Computed tomography (CT) imaging is commonly used in radiotherapy for treatment planning and dose delivery. However, magnetic resonance imaging (MRI) can offer unique advantages. The aim of the present study was to evaluate the improvement of treatment planning for patients at Shahid Rajaei Hospital, Babolsar, Iran by fusing images from both imaging modalities and evaluating the dose variation to the sensitive eye area of these patients.

**Methods and Materials:** In this case-control study, 30 patients with glioblastoma multiforme (GBM) who underwent CT scan and MRI were selected for the study. For each patient, two separate treatment plans were performed: One using a combination of CT scan and MRI images and another using CT scan images only. For each treatment plan, one set of data representing the clinical tumor volume values and a second set representing the dose received in the sensitive area of the right and left eyes were extracted and subjected to statistical comparison.

**Results:** According to the data obtained from the dual-modality and single-modality treatment plans, there was

a significant difference between the data in both treatment phases ( $P \leq 0.05$ ). Due to the ability of MRI to display soft tissue and edema around the tumor, the clinical volume of the tumor treatment plan increases in the dual-modality treatment plan compared to the single-modality treatment plan. The results of dosimetry of the sensitive eye area showed that when using MRI images, the dose received by the sensitive eye area increases in most patients.

**Conclusions:** According to the results of this study, the dual-modality treatment plan improves the patient's radiotherapy by increasing the clinical tumor volume compared to the single-modality treatment plan. Additionally, the average and mean dose received by the sensitive eye area of patients increases in the dual-modality treatment plan.

**Keywords:** Glioblastoma Multiform, Treatment Plan, GBM, MRI

### ■ Nested-CNN: An Architecture for Prediction of Three-Dimensional Dose Distribution for Prostate Cancer in Tomo-helical Technique

Maryam Zamanian<sup>1</sup>, Maziar Irannejad<sup>2</sup>, Mohsen Saeb<sup>1,3</sup>, Mahnaz Roayaei<sup>4</sup>, Iraj Abedi<sup>1\*</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>2</sup>Department of Electrical Engineering, Najafabad Branch, Islamic Azad University, Najafabad, Iran

<sup>3</sup>Department of Radiation Oncology, Isfahan Seyed-alshohada Hospital, Isfahan, Iran

<sup>4</sup>Department of Radiation Oncology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

\* Corresponding Author: Department of Medical Physics, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. Email: zamaniamary38@gmail.com

#### Abstract

**Background:** Modifying network layers to increase the accuracy of dose distribution prediction, rather than increasing their dimensions which requires complex calculations, has led to the development of new networks. One such network is nested-UNet, whose performance was compared to UNet in the current study.

**Methods and Materials:** A total of 137 prostate cancer patients treated with the tomotherapy technique were categorized as 80% training and validation (8-fold cross-validation) and 20% testing for the nested-UNet and UNet architectures. The network training was optimized using the ADAM algorithm and Dice loss function, with a learning rate of 0.003. Mean absolute percentage error (MAPE) was used to measure the dosimetry indices of dose-volume histogram (DVH) curves and geometry indices, including Structural Similarity Index Measure (SSIM), Dice similarity coefficient (DSC), and Jaccard similarity coefficient (JSC) for the isodose volumes (IVs) similarity prediction. To verify the statistically significant difference, the two-way statistical Wilcoxon test was used at a level of 0.05 ( $P < 0.05$ ).

**Results:** The overall mean of MAPE for the planned target

volume (PTV) was  $2.58 \pm 2.01$  vs.  $1.34 \pm 1.60$  and for organs at risk (OARs) was  $6.95 \pm 0.17$  vs.  $2.10 \pm 0.15$  for standard UNet and nested-UNet, respectively. In both networks, the MAPE Index for PTV includes  $D2\% = 2.19 \pm 1.47$  vs.  $1.48 \pm 1.06$ ,  $D98\% = 2.90 \pm 2.49$  vs.  $1.70 \pm 1.58$ , and for OARs: V70Gy in the rectum ( $10.05 \pm 5.29$  vs.  $5.89 \pm 3.21$ ) and bladder ( $9.80 \pm 5.28$  vs.  $4.11 \pm 2.20$ ), and V23Gy in the right ( $5.47 \pm 3.61$  vs.  $2.96 \pm 2.06$ ) and left ( $6.75 \pm 3.74$  vs.  $3.63 \pm 2.72$ ) femoral heads were significantly different ( $P < 0.05$ ). Additionally, the greatest geometric similarity was observed in the mean SSIM ( $0.94 \pm 0.01$  vs.  $0.97 \pm 0.01$ ) for standard UNet and nested-UNet, respectively.

**Conclusions:** The nested UNet network can be considered a suitable network due to its ability to improve the accuracy of dose distribution prediction compared to the UNet network in an acceptable time.

**Keywords:** Dose Distribution Prediction, Nested-UNet, UNet

### ■ Magnetic Field-Induced Reversible Blood-Brain Barrier Permeabilization: Enhancing Drug Delivery for Brain Tumor Therapy

Sahel Heydarheydari<sup>1</sup>, Mozafar Naserpour<sup>1,\*</sup>

<sup>1</sup>Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* Corresponding Author: Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: naserpour1983@gmail.com

#### Abstract

**Background:** The selective permeability of the blood-brain barrier (BBB) is essential for cellular survival, yet it poses a significant challenge for the delivery of therapeutic agents that cannot naturally cross the barrier. Magnetic permeabilization, or magneto-poration, is a physical technique that uses pulsed magnetic fields to temporarily increase the permeability of the BBB. It is classified as a drug delivery technique, offering benefits such as deep magnetic field penetration, non-invasiveness, safety, and cost-effectiveness compared to other permeabilization approaches. This systematic review examines the use of magnetic field-induced reversible BBB permeabilization to enhance drug delivery for brain tumor therapy, focusing on its application in magnetochemotherapy.

**Methods:** A systematic literature search was conducted without time restriction, using databases such as Scopus, PubMed, and Web of Science. Citation tracking tools such as PubMed and Google Scholar were also utilized to ensure a comprehensive search. The inclusion criteria were limited to original, peer-reviewed studies published in English. The quality of the selected articles and the risk of bias were assessed following the PRISMA 2020 guidelines.

**Results:** This systematic review highlights that repetitive transcranial magnetic stimulation (rTMS) effectively induces reversible modulation of the BBB, as evidenced

by animal and human studies. Animal studies reported increases of 18.5% and 6.93% at 1 Hz and 10 Hz, respectively, while a human trial found significant permeability increases in 10 out of 15 glioblastoma patients following 1 Hz stimulation. A 28-pulse, 1 Hz protocol significantly enhanced Evans blue uptake ( $P < 0.001$ ), with peak permeability at 30 - 60 minutes and reversibility within 24 hours. Intensities at or above 100% of the resting motor threshold (RMT) also increased permeability ( $P < 0.05$ ). These findings highlight the potential of specific rTMS protocols for controlled BBB modulation.

**Conclusions:** By combining magnetoporation with chemotherapy, magnetochemotherapy emerges as a novel tumor treatment, enhancing drug uptake through increased BBB permeability. High-intensity magnetic fields improve therapeutic efficacy, reduce costs, and minimize side effects, offering a promising alternative to conventional therapies.

**Keywords:** Brain Tumor, Drug Delivery, Blood-Brain Barrier, Magnetic Permeabilization

### ■ Radiation Shielding Requirements for Designing a Halcyon Linac Vault: A Compliance with IAEA SRS-47

Abolfazl Kanani <sup>1,\*</sup>, Najmeh Ghatei <sup>1</sup>

<sup>1</sup>Pardis Cancer Research Center, Pardis Cancer Institute, Shiraz, Iran

\* *Corresponding Author:* Pardis Cancer Research Center, Pardis Cancer Institute, Shiraz, Iran. Email: en.a.kanani@gmail.com

#### Abstract

**Background:** Varian recently introduced Halcyon, a fast-rotating coplanar O-ring linear accelerator (Linac) for conventionally fractionated image-guided radiation therapy (IGRT). This innovative Linac was developed with strict performance specifications to enhance patient safety and treatment accuracy. It features a 6 MV single-energy flattening filter-free (FFF) beam with a maximum field size of 28 × 28 cm<sup>2</sup> at isocenter. Moreover, it offers a fast gantry rotation speed of four revolutions per minute. This O-ring design necessitates distinct shielding requirements, similar to those observed in tomotherapy units. To minimize vault shielding requirements, the Halcyon has a beam stopper with a transmission of 0.1%. The present study primarily aimed to evaluate the shielding requirements for the Halcyon linac, taking into account the beam stopper and high throughput, while addressing certain shortcomings in current guidelines.

**Methods:** The IAEA safety report No. 47 was applied to calculate primary and secondary barriers, taking into account geometric parameters, use and occupancy factors, as well as workload estimates. Historical treatment records were utilized to determine the primary and leakage workloads. Additionally, the beam stopper was factored into the calculation of the primary barriers.

**Results:** The maximum number of patients treated in a

single day was assumed to be 70, which was then used to calculate the primary workload at 3 Gy/patient. The primary and leakage workloads are  $1.2 \times 10^5$  cGy/wk and  $3.6 \times 10^5$  cGy/wk at 1 m, respectively. For our vault, the primary barriers were found to require 2.5, 2.36, and 2.33 tenth-value layers (TVLs) of shielding. The secondary barriers for other walls required 3.1 and 3.31 TVLs.

**Conclusions:** The Halcyon design with its unique beam stopper reduces primary leakage, which is the dominant contributor to radiation exposure. Therefore, shielding requirements for the Halcyon vault can be reduced by up to 3.5 TVLs. This significantly reduces construction costs for clinics. Additionally, future regulatory standards and shielding guidelines should consider the correct use and intensity-modulated radiation therapy (IMRT) factors for advanced techniques such as IMRT, volumetric modulated arc therapy (VMAT), stereotactic body radiation therapy (SBRT), and stereotactic radiosurgery (SRS). It is also crucial to apply the appropriate TVL value for a 6 MV-FFF X-ray beam.

**Keywords:** Halcyon Linac, Radiation Shielding, SRS-47

### ■ Optimization of Hybrid Arc Treatment Planning Based on IMRT and VMAT for Nasopharyngeal Cancer

Saeedeh Moharramkhani <sup>1,\*</sup>, Ghazale Geraily <sup>1</sup>, Reza Ghalehtaki <sup>2</sup>

<sup>1</sup>Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Radiation Oncology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences, Tehran, Iran. Email: saieadehmoharramkhani@yahoo.com

#### Abstract

**Background:** Nasopharyngeal carcinoma (NPC) is a prevalent head and neck malignancy. Due to the complex anatomy, surgery is not typically the primary treatment option, leading to radiotherapy remaining the mainstay of treatment. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) are recognized as key methods in NPC management. The hybrid arc technique, which combines the advantages of both methods, has the potential to improve dose distribution. The present study aims to determine the optimal weighting of IMRT and VMAT techniques in hybrid arc treatment planning and propose a comprehensive weighting protocol for NPC management.

**Methods:** For 10 NPC patients, 11 hybrid treatment plans with varying weight combinations were developed using the Monaco treatment planning system. Weighting was performed by assigning different fraction numbers to each method, with proportions varying from 0% to 100% in steps of 10%. The IMRT component included 9 fields, while the VMAT component consisted of 2 full arcs. The optimal weight combination was determined based on

the dose received by organs at risk (OARs), including the brainstem, spinal cord, optic nerves, optic chiasm, parotid glands, larynx, oral cavity, brachial plexus, cochlea, lacrimal glands, esophagus, temporal lobes, eyes, pharyngeal constrictor muscle, and lenses. Coverage of PTV70, PTV64, and PTV56 was also assessed. Additionally, heterogeneity and conformity indexes, treatment time, and monitor units (MUs) were analyzed to present an optimal weighting protocol.

**Results:** The findings indicate that utilizing a suitably weighted hybrid plan can significantly enhance treatment plan quality. A 50:50 weighting is recommended when prioritizing OAR preservation, while weightings between 10:90 and 30:70 favoring VMAT can be considered optimal when prioritizing PTV coverage. A 40:60 weight combination can serve as an optimal balance among all parameters influencing treatment plan quality.

**Conclusions:** Coverage of PTV70, PTV64, and PTV56, as well as monitor units (MUs), significantly decreased with an increase in IMRT weighting ( $P = 0.003$ ,  $P < 0.001$ ). Conversely, the conformity index (CI), Heterogeneity Index (HI), and treatment time improved with an increased share of VMAT ( $P < 0.005$ ). The dose received by most organs at risk (OARs) in the hybrid plan with a 50:50 weighting was minimized.

**Keywords:** Hybrid Plan, IMRT, VMAT, Nasopharyngeal Cancer, NPC

## ■ The Upright Radiotherapy Technique Versus the Conventional Supine Method for Lung Cancer Treatment and Imaging: A Systematic Review

Mohammad Reza Mohammadpour <sup>1,2,\*</sup>, Marziyeh Tahmasbi <sup>2</sup>

<sup>1</sup>Students Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Radiologic Technology, School of Allied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* Corresponding Author: mr.mohammadpour1382@gmail.com

### Abstract

**Background:** Lung cancer treatment poses significant challenges due to high mortality rates, even in developed nations. There exists considerable bias and uncertainty in treatment approaches for this cancer. Therefore, developing techniques to improve treatment results is essential. This systematic review aims to evaluate the potential advantages of the new emerging technique referred to as upright radiotherapy compared to the conventional supine position in radiotherapy and imaging for lung cancer patients.

**Methods:** A comprehensive search of PubMed, Science Direct, Web of Science, and Google Scholar databases up to December 2024 was conducted. Various combinations of keywords, including "lung cancer", "upright radiotherapy technique", and "imaging", were utilized. Finally, 16 of

the most recent and relevant records were included in the study.

**Results:** Based on the reviewed records, the magnitude of motion inside the lung was smaller and the lung volume was larger in the upright position for radiation therapy (both standing and sitting positions) compared to the supine position. Although the inspiratory volumes of the total lung, right lung, left lung, and all lobes were similar for the standing and sitting positions, some studies indicated that the inspiratory and expiratory airway volumes and luminal areas of the trachea, bilateral main bronchi, and average third-generation airway were significantly higher in the upright position (standing and sitting positions) than in the supine position treatment. Furthermore, both blood flow and ventilation were greater in the caudal regions of the lungs with upright treatment. The redistribution was greater for blood flow than for ventilation, resulting in decreasing ventilation-to-perfusion ratios down the lung when upright.

**Conclusions:** The reviewed results suggest that the upright radiotherapy technique may offer clinical benefits, including reduced respiratory motion, enhanced patient comfort, decreased normal tissue irradiation, and reduced size and complexity of radiotherapy machines. This approach holds promise for improving the quality of cancer treatment while potentially lowering costs associated with radiotherapy facilities. Further research is warranted to validate these findings and explore the broader clinical implications of the upright technique in lung cancer treatment.

**Keywords:** Lung Cancer, Upright Radiotherapy, Imaging

## ■ Comparative Analysis of Manual and AI-Based Contouring for Mandible, Oral Cavity, and Parotid Glands in Head and Neck Radiotherapy

Hossein Rast <sup>1,\*</sup>, Zahra Pourparvar <sup>1</sup>, Nahid Shami <sup>1</sup>, Farzaneh Haj Alikhani <sup>1</sup>, Alireza Amouheidari <sup>1</sup>

<sup>1</sup>Department of Radiation-Oncology, Isfahan Milad Hospital, Isfahan, Iran

\* Corresponding Author: Department of Radiation-Oncology, Isfahan Milad Hospital, Isfahan, Iran. Email: rast.hossein@gmail.com

### Abstract

**Background:** Accurate delineation of the mandible, oral cavity, and parotid glands is crucial in head and neck cancer radiotherapy to minimize damage to surrounding healthy tissues. Manual contouring, though standard, is time-consuming and prone to inter-observer variability. Artificial intelligence (AI)-based auto-contouring offers a potential solution, improving efficiency and consistency.

**Method:** This review compares manual and AI-based contouring methods for the mandible, oral cavity, and parotid glands, focusing on accuracy, efficiency, and clinical relevance. We evaluate studies using convolutional neural networks (CNNs) and other deep learning techniques for

AI-driven contouring. Metrics such as Dice similarity coefficients (DSC), contouring time, and inter-observer variability are analyzed to highlight the strengths and limitations of both approaches.

**Result:** The AI-based contouring has shown comparable or superior accuracy to manual methods, especially for the mandible and parotid glands, with DSC scores often exceeding 0.85. While AI models for the oral cavity show promising results, anatomical variability presents challenges. The AI systems significantly reduce contouring time and improve consistency, addressing many of the limitations of manual contouring. However, these systems require large, high-quality annotated datasets and may still need clinician supervision for complex cases.

**Conclusions:** The AI-based contouring can enhance the accuracy, efficiency, and reproducibility of radiotherapy planning for head and neck cancers. Despite its potential, further validation, robust datasets, and model refinement are necessary for clinical implementation, especially for complex anatomical structures like the oral cavity. Future research should focus on improving model generalization and clinical reliability.

**Keywords:** Manual Contouring, AI-based Contouring, Head and Neck Cancer, Radiotherapy, Treatment Planning

### ■ MRI Radiomics for Prediction of Response to Neoadjuvant Chemotherapy in Patients with Muscle-Invasive Bladder Cancer

Abolfazl Razzaghdoust<sup>1,\*</sup>, Bahram Mofid<sup>2</sup>, Benyamin Khajetash<sup>3</sup>, Hamid Abdollahi<sup>4,5</sup>, Bahareh Hatami<sup>6</sup>, Anya Jafari<sup>2</sup>, Abbas Basiri<sup>1</sup>, Arash Mahdavi<sup>7</sup>

<sup>1</sup>Urology and Nephrology Research Center, Research Institute for Urology and Nephrology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Radio-Oncology, Shohada-e Tajrish Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Medical Physics, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Radiology, University of British Columbia, Vancouver, Canada

<sup>5</sup>Department of Integrative Oncology, BC Cancer Research Institute, Vancouver, Canada

<sup>6</sup>Department of Radiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>7</sup>Department of Radiology, University of Washington School of Medicine, Washington, United States

\* *Corresponding Author:* Urology and Nephrology Research Center, Research Institute for Urology and Nephrology, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: razzaghdoust@yahoo.com

#### Abstract

**Background:** The clinical application of an imaging biomarker for identifying muscle-invasive bladder cancer (MIBC) patients who respond to neoadjuvant chemotherapy (NAC) could assist clinicians in avoiding unnecessary chemotherapy and its associated complications in patients unlikely to derive clinical benefit. Recent research has demonstrated the utility of MRI-based radiomics in predicting tumor response to NAC across various cancer types. Therefore, this prospective study aimed to employ

different MRI-based radiomics models to predict the clinical complete response (CR) of MIBC patients.

**Methods:** The MIBC patients eligible for platinum-based NAC from two tertiary referral hospitals were prospectively included in this study. Regions of interest (ROIs) on each tumor were manually annotated in various pre-treatment MR images, including contrast-enhanced T1-weighted imaging (CE-T1WI), T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) maps. The primary objective was to assess the clinical CR to chemotherapy. A Python package was utilized for radiomics feature extraction, and the least absolute shrinkage and selection operator (LASSO) was applied for feature selection. A stratified K-fold cross-validation approach with five splits was employed to ensure robust evaluation. Several machine learning algorithms were utilized to develop predictive models based on different MRI sequences, ADC maps, and clinical factors. The performance of these models was evaluated using a comprehensive set of metrics to ensure a robust analysis of classification effectiveness.

**Results:** Out of 62 recruited patients, 52 cases with available pre-treatment MRI and response status were deemed eligible for inclusion in the analysis. After chemotherapy, clinical CR was achieved in 19 patients (37%). A total of 177 radiomics features were extracted for this study. Based on the area under the receiver operating characteristic curve (AU-ROC) metric, the best performance among 30 different models was observed with the support vector machine (SVM) classifier using selected features derived from CE-T1WI (AUC = 0.88), yielding sensitivity, specificity, and precision values of 0.82, 0.79, and 0.79, respectively. A model based on the k-nearest neighbors (KNN) classifier performed second best using the selected features extracted from the CE-T1WI sequence (AUC-ROC = 0.87; sensitivity = 0.94; specificity = 0.70; precision = 0.76).

**Conclusions:** The MRI-based radiomics shows promise for noninvasively predicting the NAC response in MIBC patients. Further larger studies are necessary to confirm these findings.

**Keywords:** Radiomics, MIBC, Neoadjuvant Chemotherapy, Response Prediction

### ■ Stereotactic Body Radiation Therapy for Lung Cancer Treatment: A Systematic Review

Rahele Kazemi<sup>1,2,\*</sup>, Marziyeh Tahmasbi<sup>2</sup>

<sup>1</sup>Students Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Radiologic Technology, School of Allied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* *Corresponding Author:* Rahele.k200@gmail.com

#### Abstract

**Background:** Stereotactic body radiation therapy (SBRT) has emerged as a precise and effective treatment modal-

ity for lung, prostate, liver, and pancreatic cancers, as well as spine, neck, and lymph nodes, leveraging advanced imaging techniques and highly focused radiation beams to deliver ablative doses. This systematic review evaluates the clinical efficacy, advantages, and limitations of SBRT in treating early-stage lung cancer and lung oligometastases. The ability of SBRT to minimize damage to healthy tissues while achieving high local control rates makes it a valuable option for patients unsuitable for surgery or those with inoperable tumors. A comprehensive literature review of recent studies on SBRT, focusing on treatment outcomes, toxicity profiles, and patient selection criteria was carried out. Key parameters analyzed included radiation dosage, treatment duration, and the role of concurrent therapies. Special attention was given to SBRT applicability in central and ultra-central lung tumors, where toxicity risks remain challenging.

**Methods:** PubMed, Science Direct, Web of Science, and Google Scholar databases were explored up to October 2024, using different combinations of the keywords: "Stereotactic Body Radiation Therapy", "SBRT", "Treatment Outcome", "Early-Stage", "Oligometastatic", and "Lung Cancer". Finally, 10 of the most recent and relevant records were included in the study.

**Results:** The reviewed records demonstrated that SBRT offers high local tumor control and low toxicity rates in early-stage and oligometastatic lung cancers. However, potential adverse effects, including pneumonitis and esophagitis, necessitate careful patient selection and individualized treatment planning. The reviewed records highlighted the adaptability of SBRT in treating tumors near critical structures through advanced techniques like proton beam therapy.

**Conclusions:** Based on the results of the reviewed records, it can be concluded that SBRT is a viable alternative to surgery for lung cancer patients, providing effective tumor control with reduced treatment durations. Nevertheless, the application of SBRT for supracentral tumors demands caution due to higher toxicity risks. Future research should explore optimizing SBRT protocols and integrating immunotherapy to enhance outcomes.

**Keywords:** Stereotactic Body Radiation Therapy (SBRT), Treatment Outcome, Lung Cancer

## ■ Artificial Intelligence Techniques to Predict Breast Cancer Recurrence Risk: A Systematic Review

Rahele Kazemi<sup>1,2,\*</sup>, Mohammad Reza Mohammadpour<sup>1,2</sup>, Marziyeh Tahmasbi<sup>2</sup>

<sup>1</sup>Student Research Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Radiologic Technology, School of Allied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* Corresponding Author: rahele.k200@gmail.com

### Abstract

**Background:** Breast cancer is the most common disease

among women worldwide and the second leading cause of death. Breast cancer clinicians need accurate tools to aid in clinical decision-making and to detect and predict cancer recurrence. Today, a new era has begun with the emergence of artificial intelligence (AI), particularly in image analysis, which paves the way for major advances in breast cancer diagnosis and predicting the risk of cancer recurrence. For patients with breast cancer, AI methods can help with screening, diagnosis, staging, biomarker assessment, prognosis, and prediction of treatment response or tumor recurrence. AI algorithms can be used to predict cancer risk using patient history, scans, imaging information, and specific cases. In this systematic review, the most common AI algorithms used for predicting breast cancer recurrence have been discussed.

**Methods:** The PubMed, Science Direct, Web of Science, and Google Scholar databases were explored up to October 2024 using various combinations of keywords: "breast cancer", "artificial intelligence", "machine learning", "deep learning", "recurrence risk prediction" and "treatment response assessment". Finally, the most recent and relevant records were included in the study.

**Results:** The reviewed literature showed that machine learning models are more widely used (83.9%) than deep learning models (16.1%) in predicting breast cancer recurrence risk. Among machine learning methods, the support vector machine (SVM) algorithm is the most commonly used model to predict breast cancer recurrence risk, with the maximum reported accuracy of 0.957 and sensitivity of 0.971. The SVM algorithm is a supervised machine learning model. The reason for the popularity of this algorithm can be its reliability and ability to work with small data volumes, especially in cases where pattern recognition is required.

**Conclusions:** Based on the results obtained from the reviewed records, it can be concluded that the most common artificial intelligence algorithm with the highest prediction accuracy is the SVM method. The AI methods can help expedite breast cancer recurrence risk assessment or treatment response evaluation.

**Keywords:** Breast Cancer, Artificial Intelligence, Machine Learning, Deep Learning, Cancer Recurrence, Prediction, Treatment Response

## ■ Evaluation of Correlation of MVCT-based Radiomics Features and Radiation Dose in Tomotherapy

Davood Khezerloo<sup>1,2,\*</sup>, Amin Poorfarshid<sup>2</sup>, Soheila Sharifian-jazi<sup>3</sup>, Amir Ghasemi-jangjoo<sup>2</sup>, Masoumeh Khani<sup>4</sup>

<sup>1</sup>Department of Radiology, Faculty of Alliance Medical Sciences, Tabriz University of Medical Science, Tabriz, Iran

<sup>2</sup>Department of Radio-Oncology, Faculty of Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>3</sup>Department of Medical Physics, Faculty of Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>4</sup>Department of Radiology, Madani Educational Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

\* Corresponding Author: D.khezerloo@gmail.com

## Abstract

**Background:** It is believed that medical images contain pathophysiological information that is hidden from the naked eye. Radiomics is an emerging field that converts image data into highly meaningful features. After irradiation, tissue morphology and pathology undergo changes. In this study, we aimed to determine if megavoltage computed tomography (MVCT)-based radiomics features are sensitive to radiation dose delivery during the tomotherapy procedure.

**Methods:** In this retrospective study, the correlation between radiomics features and radiation dose delivery during early treatment sessions was investigated. Tomotherapy MVCT images from 10 brain cancer patients, whose treatment had been completed, were selected for radiomics evaluation. During radiomics analysis, a circular 2D region of interest (ROI) with a constant diameter was delineated inside brain tissue within the 90% isodose. The second-order radiomics features from the MVCT images during the first, fifth, and tenth treatment fractions were extracted using Pyradiomics toolkits. Finally, the correlation between radiomics feature values and fraction numbers was assessed using the Spearman correlation coefficient.

**Results:** A total of 22 second-order texture features were extracted. These features were divided into 7 gray-level co-occurrence matrix (GLCM), 1 gray-level run length matrix (GLRLM), 3 neighboring gray-level dependence matrix (NGLDM), and 11 gray-level zone length matrix (GLZLM). Eight radiomics features between treatment fractions showed a very high Spearman correlation coefficient (> 0.75): GLCM homogeneity (0.86), GLCM energy (0.76), GLCM contrast (0.79), GLCM dissimilarity (0.79), GLRLM run percentage (RP) (0.85), NGLDM coarseness (0.79), NGLDM contrast (0.79), and NGLDM busyness (0.75).

**Conclusions:** In this study, several GLCM radiomics features showed strong correlations during early treatment fractions. Previous studies have utilized high-quality MRI or kilovoltage CT (kVCT) for similar analyses; however, MVCT in tomotherapy is a standard routine procedure during radiotherapy. During early treatment fractions, radiomics can evaluate treatment response and personalize treatment schedules.

**Keywords:** Radiomics, Radiotherapy, Tomotherapy, MVCT, Radiation Dose, Treatment Fraction

## ■ Comparison of Hypofunction Radiotherapy with Conventional Radiotherapy in Breast Cancer Based on Radiobiological Modeling of TCP and NTCP

Bahare Arjmand <sup>1,\*</sup>, Nahid Chegini <sup>1</sup>

<sup>1</sup>Department of Medical Physics, Faculty of Medicine, Ahvaz Jundishapur University of

Medical Sciences, Ahvaz, Iran

\* Corresponding Author: Department of Medical Physics, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: baharearjmand84@gmail.com

## Abstract

**Background:** The present study uses radiobiological models to optimize treatment design by calculating and comparing the probability of tumor control and the probability of complications in healthy tissue in conventional three-dimensional conformal radiation therapy (3D-CRT) and hypofractionation regimens for breast cancer radiotherapy.

**Methods:** Clinical data from the treatment plans of 30 patients with left breast-conserving surgery were analyzed for three different hypofractionation regimens (39 Gy and 41.6 Gy in 13 sessions and 40 Gy in 15 sessions) and a common treatment regimen (50 Gy in 25 sessions). Dose-volume histogram (DVH), dosimetry, and radiobiological parameters were measured and compared for the target volume of the planning target volume (PTV) (left breast) and the two organs at risk: The heart and left lung.

**Results and Conclusions:** In general, hypofractionation regimens showed the least side effects in the heart and lung tissue, particularly in the regimen of 39 Gy in 13 fractions. However, in terms of breast tumor control, there was no significant difference compared to the conventional regimen.

**Keywords:** Breast Cancer, Hypofraction Regimen, Radiotherapy

## ■ Deep Learning in Neuro-Oncological Imaging: Point Transformer Versus U-Net for Precise Brain Tumor Delineation - A 341-Patient Clinical Study

Abolfazl Koozari <sup>1</sup>, Mohammadreza Elhaie <sup>2,\*</sup>, Nadia Nadia Najafi Zade <sup>3</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Department of Medical Physics, School of Medicine Isfahan University of Medical Sciences, Isfahan, Iran

<sup>3</sup>Department of Radiation Oncology, School of Medicine, Isfahan University of Medical Science, Isfahan, Iran

\* Corresponding Author: Department of Medical Physics, School of Medicine Isfahan University of Medical Sciences, Isfahan, Iran. Email: mreelhaie@gmail.com

## Abstract

**Background:** Brain tumor segmentation accuracy significantly impacts treatment planning and surgical guidance. While U-Net has been a standard architecture in medical image segmentation, point transformer represents a newer approach leveraging spatial attention mechanisms. This study presents a direct comparison between these two architectures in brain tumor segmentation tasks, evaluating their performance across a large patient cohort.

**Methods:** In this study, we conducted a comprehensive analysis of magnetic resonance imaging (MRI) datasets obtained from a cohort of 341 patients with histopathologically confirmed brain tumors. Two distinct deep learning architectures were implemented and systematically evaluated under standardized conditions: A point transformer model incorporating spatial attention mechanisms and a conventional U-Net architecture featuring skip connections. Model performance assessment was executed through a rigorous 5-fold cross-validation protocol, employing quantitative metrics including Dice similarity coefficient (DSC), sensitivity, specificity, and computational efficiency metrics. The evaluation framework was designed to ensure statistical robustness while maintaining consistent preprocessing parameters and hardware configurations across both architectures to facilitate direct comparative analysis.

**Results:** Quantitative analysis revealed that the point transformer architecture achieved statistically significant superiority across multiple performance metrics, demonstrating a Dice similarity coefficient of 0.85 compared to U-Net's 0.83 ( $P < 0.01$ ), enhanced sensitivity (0.88 vs 0.84,  $P < 0.01$ ), and improved specificity (0.92 vs 0.89,  $P < 0.01$ ). Conversely, the U-Net architecture exhibited notable advantages in computational efficiency parameters, including substantially reduced processing time (1.8 seconds/scan compared to point transformer's 3.1 seconds/scan), 40% lower GPU memory utilization, and superior training dynamics characterized by accelerated convergence rates. These findings suggest a clear trade-off between segmentation accuracy and computational resource requirements between the two architectures.

**Conclusions:** Point transformer achieves higher segmentation accuracy, particularly in complex tumor boundaries, showing a 2% improvement in Dice coefficient over U-Net. However, this comes at the cost of increased computational demands and longer processing times. The choice between these architectures may depend on specific clinical requirements, balancing accuracy needs against computational resource constraints.

**Keywords:** Brain Neoplasms, Magnetic Resonance Imaging, Deep Learning, Image Segmentation, Neural Networks

## ■ A Hybrid Deep Learning Model for Enhanced Multi-Organ Segmentation in Prostate Cancer Radiotherapy

Najmeh Arjmandi <sup>1,2</sup>, Mehdi Momennezhad <sup>1</sup>, Shahrokh Nasserri <sup>1</sup>, Mohammad Amin Mosleh Shirazi <sup>2,3</sup>, Amin Amiri Tehranizadeh <sup>4</sup>

<sup>1</sup>Department of Medical Physics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Physics Unit, Department of Radio-Oncology, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>3</sup>Ionizing and Non-ionizing Radiation Protection Research Center, School of Paramedical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Department of Medical Physics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: n.arjmandi.b@gmail.com

### Abstract

**Background:** The present study investigates the efficacy of hybrid deep learning architectures for automated multi-organ segmentation in prostate cancer radiotherapy planning. We compare a modified TransFuse model, a Swin-U-Net model, and a modified residual U-Net.

**Methods:** We utilized a dataset comprising planning CT images from 104 early-stage prostate cancer patients. The TransFuse model integrates both convolutional and transformer features to capture local and global dependencies, while the Swin-U-Net employs a fully transformer-based approach to leverage long-range contextual information. We evaluated the segmentation performance of these models using metrics such as Dice similarity coefficient (DSC), Hausdorff distance (HD), and relative volume difference (RVD).

**Results:** The modified TransFuse model achieved a DSC of 90.34% for prostate segmentation, surpassing both Swin-U-Net (89.16%) and a modified residual U-Net (88.10%). This improved performance, attributed to its effective integration of local and global features, consistently outperformed these models across multiple organ segmentations.

**Conclusions:** The superior performance of the modified TransFuse model suggests that hybrid deep learning architectures offer a promising approach to improving the accuracy and efficiency of automated contouring in prostate cancer radiotherapy planning. The combined strengths of convolutional neural networks (CNNs) for capturing local details and transformers for capturing global context provide a powerful combination for this challenging task.

**Keywords:** Modified TransFuse Model, Modified Residual U-Net, Swin-U-Net, Prostate Cancer

## ■ Preparation and Quality Control of <sup>177</sup>Lu-Alpha-MSH for the Treatment of Melanoma

Samaneh Zolghadri <sup>1\*</sup>, Hassan Yousefnia <sup>1</sup>, Sara Vosoughi <sup>1</sup>, Arezou Karimian <sup>1</sup>

<sup>1</sup>Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran

\* Corresponding Author: Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran. Email: szolghadri@aeoi.org.ir

### Abstract

**Background:** Melanoma, a type of skin cancer, is less common than other types but is the most aggressive with high metastatic properties. The melanocortin type 1 receptor (MC1R) is recognized as a popular target for imaging and therapy of melanoma.  $\alpha$ -Melanocyte stimulating hormone ( $\alpha$ -MSH) has recently shown subnanomolar binding affinity to MC1R. This study aimed to develop [<sup>177</sup>Lu]- $\alpha$ -MSH for the treatment of melanoma in the country.

**Methods:**  $^{177}\text{Lu}$  and CCZ01048 were provided by Pars Isotope Company.  $^{177}\text{Lu}$ -Alpha-MSH was prepared, and several experiments were performed to determine the optimized conditions for radiolabeling. The radiochemical purity of the complex was assessed by the radio-thin layer chromatography (RTLC) and high-performance liquid chromatography (HPLC) methods. The stability of the final complex in PBS buffer and human serum was studied. Tumor implantation was performed by injecting a 50  $\mu\text{L}$  suspension of B16F10 cells (consisting of  $1 \times 10^7$  cells) subcutaneously into nude mice. The biodistribution of the complex was studied in normal and tumor-bearing mice up to 148 hours.

**Results:**  $^{177}\text{Lu}$ Lu-Alpha-MSH was prepared with a radiochemical purity of greater than 98% under optimized conditions (pH = 4.5, temperature =  $95^\circ\text{C}$ , time = 30 minutes). The high stability of the radiolabeled compound was observed in PBS buffer ( $4^\circ\text{C}$ ) and human serum ( $37^\circ\text{C}$ ). The biodistribution of the complex showed considerable accumulation in the tumor and kidneys. The results indicated the urinary tract as the major route of excretion.

**Conclusions:** The present study demonstrated the possible production of  $^{177}\text{Lu}$ Lu-Alpha-MSH and its potential utilization for the treatment of melanoma in the country.

**Keywords:** Lu-Alpha-MSH, Quality Control, Melanoma

### ■ Optimized Production of $^{68}\text{Ga}$ Ga-AMBA for GRPR-expressing Tumor Imaging

Samaneh Zolghadri <sup>1,\*</sup>, Hassan Yousefina <sup>1</sup>, Behrouz Alirezapour <sup>1</sup>, Arezou Karimian <sup>1</sup>

<sup>1</sup>Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran

\* Corresponding Author: Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran. Email: szolghadri@aeoi.org.ir

#### Abstract

**Background:** In recent decades, peptide-based radiopharmaceuticals designed to target specific receptors have demonstrated significant clinical potential. The gastrin-releasing peptide receptor (GRPR) is identified as a significant target due to its overexpression in various human tumors, including prostate, lung, breast, and pancreatic cancers. AMBA, a bombesin-derived agonist, is noted for its high affinity for GRPR and BB1 receptors, ensuring enhanced radiotracer accumulation in tumors, thereby improving cancer detection. This study aimed to develop  $^{68}\text{Ga}$ Ga-AMBA for PET imaging of GRPR-expressing tumors.

**Methods:**  $^{68}\text{GaCl}_3$  was prepared using an in-house  $^{68}\text{Ge}/^{68}\text{Ga}$  generator. The chemical and radiochemical purities were investigated using inductively coupled plasma mass spectrometry (ICP-MS) and radio thin-layer chromatography (RTLC) methods, respectively. The AMBA was labeled with  $^{68}\text{Ga}$  under optimized conditions. The radiochemical purity of the radiolabeled compound was assessed using high-performance liquid chromatography

(HPLC). The stability of the final complex was studied in PBS buffer and human serum by the RTLC method. The biodistribution of the complex was studied in normal mice.

**Results:**  $^{68}\text{Ga}$ Ga-AMBA was prepared with a radiochemical purity of greater than 98% under optimized conditions (pH = 3.5 - 4.0, reaction time = 10 minutes, and reaction temperature =  $95^\circ\text{C}$ ). The radiolabeled compound was stable in PBS buffer ( $4^\circ\text{C}$ ) and human serum ( $37^\circ\text{C}$ ) for at least 1 hour post-incubation. The biodistribution of the radiolabeled compounds in normal mice revealed rapid elimination of the activity from the blood. The highest accumulation was observed in the pancreas, an organ with high GRPR expression, indicating the effectiveness of the labeled compound for targeting GRPR-expressing tumors. Considerable accumulation was also observed in the kidney at all interval times, suggesting metabolization in the kidney and excretion through urine.

**Conclusions:** This study demonstrated the possible production of  $^{68}\text{Ga}$ Ga-AMBA and its potential utilization as a PET imaging agent for GRPR-expressing tumors in the country.

**Keywords:**  $^{68}\text{Ga}$  Ga-AMBA, PET Imaging, Radiopharmaceutical

### ■ Dosimetric Parameters Comparison of Three-Field and Field-in-Field Radiotherapy Planning in the Treatment of Glioblastoma Patients

Zeinab Alsadat Ahmadi <sup>1,\*</sup>

<sup>1</sup>Department of Radiation Therapy, Harandi Center, Isfahan, Iran

\* Corresponding Author: Department of Radiation Therapy, Harandi Center, Isfahan, Iran. Email: zs.ahmadi@yahoo.com

#### Abstract

**Background:** Glioblastoma is the most common and aggressive type of malignant brain tumor found in adults. Effective treatment options include surgical resection, radiation therapy, and chemotherapy. In most cases, glioblastoma is located near the brainstem, cerebellum, and spinal cord; therefore, radiation therapy must spare normal organs near the tumor. The current study aimed to compare dosimetric parameters in the treatment planning of three fields (3F) and three fields with one sub-field (SF) for glioblastoma patients.

**Methods:** Eight patients with glioblastoma were selected. The treatment plans were carried out using the Prowess Treatment Planning System (TPS). Two planning techniques, 3F and SF, were performed for each patient with a combination of 6 and 15-MV photon beams. Dosimetric factors were measured for planning target volume (PTV), brainstem, optic nerves, eyes, and optic chiasma. Maximum, minimum, mean dose, Homogeneity Index (HI), and Conformity Index (CI) were calculated, and the two techniques were compared using the paired t-test.

**Results:** The PTV received a lower maximum and mean dose in the SF technique compared to the 3F technique. The HI was better in the SF method than in the 3F method ( $P = 0.008$ ). The CI was smaller in the SF technique but not significantly different ( $P > 0.05$ ). For the organs at risk, the SF technique showed a reduction in the maximum dose compared to the 3F techniques, but the difference for the brainstem was not significant.

**Conclusions:** The SF technique demonstrated improved effectiveness in treating patients with glioblastoma tumors. However, the SF method requires evaluating more dosimetric parameters to determine the best approach.

**Keywords:** Three-Field, Field-in-Field, Glioblastoma, Radiotherapy Planning

## ■ Evaluating Dose Calculation Accuracy of the Monaco Treatment Planning System for Effective Wedge Angles: A Comparative Analysis of Elekta and ICRU-24 Formulas

Ali Bahari <sup>1</sup>, Mikaeil Molazadeh <sup>1\*</sup>

<sup>1</sup>Department of Medical Physics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

\* Corresponding Author: Department of Medical Physics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. Email: mikaeil.molazadeh@gmail.com

### Abstract

**Background:** Accurate dose calculation is critical in radiotherapy to ensure effective cancer treatment. The Monaco Treatment Planning System (TPS) is widely used, but its accuracy in calculating effective wedge angles (EWAs) requires thorough evaluation. This study investigates the dose calculation accuracy of the Monaco TPS for EWAs using two analytical approaches: The Elekta formula and the ICRU-24 formula.

**Methods:** Conducted at Shahid Madani Hospital, Tabriz, Iran, from September 2023 to March 2024, this experimental study computed EWAs for various field sizes ( $5 \times 5$ ,  $10 \times 10$ ,  $15 \times 15$ ,  $20 \times 20$ ,  $25 \times 25$ , and  $30 \times 30$  cm<sup>2</sup>) at nominal angles ( $15^\circ$ ,  $30^\circ$ ,  $45^\circ$ ,  $60^\circ$ ). Measurements were taken according to the Elekta and ICRU-24 guidelines, comparing TPS results with practical measurements. Dosimetry was performed with the Elekta Synergy Linac (6 MV), and readings were obtained using a Farmer ionization chamber and a 3D MP3 PTW water phantom.

**Results:** The Elekta formula exhibited consistent agreement with planned EWAs, showing deviations within  $\pm 0.5^\circ$  across all fields. In contrast, the ICRU-24 formula revealed a maximum deviation of  $\pm 2.6^\circ$ , particularly pronounced at smaller field sizes. The analysis indicated that discrepancies increased with decreasing field size and wedge angle.

**Conclusions:** The Elekta formula demonstrates superior accuracy in EWA calculations compared to the ICRU-24 formula, which showed significant variability. These find-

ings underscore the importance of selecting appropriate analytical methods for dose calculation in radiotherapy.

**Keywords:** Radiotherapy, Dose Calculation, Effective Wedge Angle, Monaco Treatment Planning System, Elekta Formula, ICRU-24 Formula

## ■ Enhancing Radiation Therapy Planning with Dual-Energy CT: Impact on Electron Density and Stopping Power Predictions

Mozafar Naserpour <sup>1\*</sup>, Sahel Heydarheydari <sup>1</sup>

<sup>1</sup>Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* Corresponding Author: Department of Medical Imaging and Radiation Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: naserpour1983@gmail.com

### Abstract

**Background:** Determining the stopping power ratio (SPR) from pre-treatment computed tomography (CT) imaging is crucial for estimating particle range and optimizing radiation therapy planning. Current SPR estimation methods using Hounsfield look-up tables (HLUT) have several limitations, such as excluding prosthetic devices, assuming uniform SPR across tissues, and lacking patient specificity. Recently, dual-energy CT (DECT) with material decomposition capabilities has emerged as a promising alternative, generating effective atomic number ( $Z_{eff}$ ) and electron density ( $\rho_e$ ) maps to enable more accurate SPR prediction and particle range calculation. This systematic review provides an in-depth analysis of the physical principles behind direct SPR measurement using DECT, the accuracy of DECT in determining ( $\rho_e$ ) and SPR, and the potential advancements this technology offers.

**Method:** A systematic literature search was conducted without time restriction, using databases such as Scopus, PubMed, and Web of Science. To ensure a comprehensive search, citation tracking tools such as PubMed and Google Scholar were also utilized. The inclusion criteria were limited to original, peer-reviewed studies published in English. The quality of the selected articles and the risk of bias were assessed following the PRISMA 2020 guidelines.

**Results:** Database searches identified 483 records, leading to the screening of 181 studies. After applying the eligibility criteria, 48 studies were included in the final analysis. The findings indicated that compared to the traditional CT number to SPR conversion, the DECT-based method demonstrated a better range of uncertainty, with values of 1% versus 3.5%. In cases where dental materials obstructed the head phantom, the DECT-based SPR prediction method exhibited a significantly stronger correlation with measured reference SPR values (deviation of 0.2 mm) than single-energy CT (SECT) predictions.

**Conclusions:** The DECT can predict SPR directly and specifically for each patient using effective atomic number and relative electron density. Despite demonstrating higher

accuracy than traditional methods, studies indicate that DECT-based methods have not yet been widely adopted in clinical settings.

**Keywords:** Dual-energy CT, Stopping Power Ratio, Particle Range Uncertainty

## ■ CT-Based Vs. MRI-Based Target Delineation: Dosimetric Outcomes in Cervical Cancer Brachytherapy

Kimiya Mohammadian <sup>1,\*</sup>, Zeinab Sadeghian <sup>1</sup>, Fatemeh Sadat Dehghan <sup>1</sup>, Mohammad Javad Enferadi- Aliabad <sup>1</sup>, Soroush Najafi Sarvestani

<sup>1</sup>Department Of Medical Physics, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

\* *Corresponding Author:* Department Of Medical Physics, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: kimiya.mohammadian@gmail.com

### Abstract

**Background:** Brachytherapy is crucial for the treatment of cervical cancer, delivering high-dose radiation to tumors while sparing healthy tissues. This review examines the differences in computed tomography (CT) and magnetic resonance imaging (MRI)-based target delineation to improve treatment strategies and outcomes.

**Methods:** Following PRISMA guidelines, PubMed and Google Scholar were searched using terms such as “CT”, “MRI” and “brachytherapy” with Boolean operators. Of 555 studies screened, five met the inclusion criteria, comparing the dosimetric impacts of MRI and CT in cervical cancer brachytherapy.

**Results:** The findings consistently demonstrate that MRI provides superior accuracy in defining high-risk clinical target volumes (CTV) compared to CT. On average, CT-defined volumes were 72% larger than MRI-defined volumes. This discrepancy underscores the tendency of CT to overestimate target volumes, potentially affecting dose delivery precision. MRI-based plans provided more reliable coverage of CTV, with 90% of patients achieving D90 > 85 Gy, compared to 80% in CT-based plans. Mean dose differences for D90, D98, and D50 between the modalities were minor, but certain outliers highlighted variability. MRI’s superior soft tissue contrast enabled more precise delineation of residual tumor regions. MRI-based plans displayed better precision for structures like the bladder, where D0.1cc were significantly higher in MRI-based plans (104 ± 11 Gy) compared to CT (98 ± 8 Gy, p = 0.012). However, differences in rectum and sigmoid doses were minimal and not statistically significant, suggesting comparable safety profiles for these organs at risk (OARs).

**Conclusions:** The MRI remains the gold standard for image-guided adaptive brachytherapy in cervical cancer. The MRI-defined target volumes provide superior dose coverage and dosimetric outcomes, ensuring optimal treatment precision. While CT-based methods offer a practical alternative in resource-limited settings, their tendency to overestimate target volumes introduces challenges in

achieving accurate dose delivery.

**Keywords:** MRI-based Radiotherapy, Cervical Cancer, CT-based, Brachytherapy

## ■ A Treatment Planning Study Comparing VMAT Techniques and Cyberknife in Single Brain Tumor: Treatment Planning Study

Mahshad Neshasteriz <sup>1</sup>, Mohsen Saeb <sup>1,\*</sup>

<sup>1</sup>Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran

\* *Corresponding Author:* Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran. Email: mohsen.saeb93@gmail.com

**Background:** Various radiation therapy techniques are currently employed for brain tumors, including intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), and CyberKnife. Modern techniques address the inefficiencies of three dimensional conformal radiotherapy (3D-CRT) by delivering higher doses to tumors while minimizing exposure to surrounding organs at risk (OARs) and reducing dosimetric and systematic uncertainties compared to 3D techniques. The present study aims to compare the dosimetric parameters and delivery efficiency of VMAT and CyberKnife in treating brain tumors of different target sizes. A comparison is presented for target coverage and delivery dose to the OARs in the treatment of brain tumors.

**Materials and Methods:** Treatment plans were generated for fifteen patients with single brain tumors, with prescribed doses ranging from 18 to 25 Gy. Treatment plans utilized Multiplan software for CyberKnife and Eclipse for RapidArc plans. The plans were generated based on the recommendations of ICRU 83 reports to achieve optimal results and were evaluated for target coverage, delivery dose to critical structures, treatment time, and brain tissue volume.

**Results:** Both modalities offer acceptable gross tumor volume coverage and OAR sparing. CyberKnife delivered a higher integral dose to the gross tumor volume and brain tissues (V12) compared to VMAT (P < 0.05). The Conformity Index was slightly better in VMAT (1.11 ± 0.25) compared to CyberKnife (1.25 ± 0.12). However, CyberKnife demonstrated a better dose Gradient Index (4.52 ± 0.99) compared to VMAT (8.6 ± 7.28). The treatment time for VMAT was significantly lower compared to CyberKnife (P < 0.05). The VMAT offered lower minimum and maximum doses to some OARs, although some differences were not statistically significant. For normal brain tissues, V12Gy was significantly lower with VMAT (3.27 ± 2.92) compared to CyberKnife (4.09 cc ± 3.27).

**Conclusions:** The VMAT technique is capable of achieving similar treatment quality as CyberKnife systems for stereotactic radiosurgery (SRS) treatments. CyberKnife is a superior modality for delivering SRS to brain tumors, except for dose homogeneity, where VMAT achieved better results. Additionally, VMAT can achieve lower integral doses to OARs and brain tissues.

**Keywords:** Stereotactic Radiosurgery (SRS), CyberKnife (CK), VMAT, Linear Accelerators (linacs)

## ■ Effect of Deep Inspiration Breath-Hold (DIBH) in Dose of Heart, Lungs, and Left Anterior Descending Artery in the Left Sided Breast Cancer Radiotherapy

Mahshad Neshasteriz<sup>1</sup>, Safoora Nikzad<sup>2</sup>, Hosein Taheri<sup>3</sup>, Mohsen saeb<sup>1,\*</sup>

<sup>1</sup>Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran

<sup>2</sup>Department of Medical Physics, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>3</sup>Department of Medical Physics, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

\* Corresponding Author: Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran. Email: mohsen.saeb93@gmail.com

### Abstract

**Background:** Cardiac and lung toxicity are long-term complications of left breast radiation therapy (BRT). Various techniques have been developed to reduce the absorbed dose to the heart, the arteries connected to it, and the lungs during breast cancer radiation treatments. The present study aimed to evaluate the dose to the lungs, heart, and left anterior descending (LAD) artery using the deep inspiration breath-hold (DIBH) technique in radiation therapy for patients with left breast cancer and compare the results with free-breathing (FB) treatment.

**Methods:** Ten patients with similar clinical conditions who underwent mastectomy surgery and could hold their breath for at least 20 seconds were included in the study. A SIEMENS CT simulator was used for CT simulation, and an Elekta Versa HD linear accelerator (Linac) was used for treatment. The Monaco treatment planning system (TPS) with the collapse cone algorithm (CC) was used for dose calculations in both DIBH and FB methods. Parameters such as volume, minimum dose, maximum dose, mean dose, V25%, V20%, V10%, V5%, and V2% were calculated for the heart, left lung, right lung, clinical target volume (CTV), LAD, and right breast. Dose-volume histograms (DVH) were measured for all mentioned organs. For the DIBH study, a special mouthpiece was used during the coaching stage for each patient, ensuring they held their breath for at least 20 seconds during CT simulation and treatment. Cone beam CT (CBCT) and/or orthogonal X-rays were applied to match patient positioning during treatment.

**Results:** All treatment plans achieved suitable planning target volume (PTV) coverage. Results indicated that the average volumes of the heart, CTV, and right breast in the FB technique were significantly higher than in the DIBH method, while there were no significant differences in the volume of the LAD, and the volume of the right and left lung were higher in DIBH. There were no significant differences in the minimum and maximum doses of organs between the two methods. The mean heart and left lung doses in the FB technique were 9.3 Gy and 11.34 Gy, re-

spectively, while for the DIBH technique, they were 3.8 Gy and 11 Gy, respectively. Furthermore, the mean dose of the LAD in the FB (47 Gy) and DIBH (25.3 Gy) techniques were significantly different ( $P < 0.001$ ) in comparison with each other. There were not any significant differences for other organs, and mean dose of CTV was significantly higher in DIBH.

**Conclusions:** For breast cancer patients, the deep inspiration breath-hold (DIBH) method may reduce the dose to organs at risk (OARs) such as the heart, left anterior descending (LAD) artery, and lungs. This reduction may potentially decrease the probability of adverse effects, including cardiac morbidity and mortality, compared to the free-breathing (FB) method. Additionally, the coverage of the clinical target volume (CTV) appears to be better with the DIBH method than with the FB method.

**Keywords:** Breast Cancer, Deep Inspiration Breath-Hold, Free Breathing, Radiotherapy

## ■ Comparison of Dose Volume Histograms of Three Whole Breast Radiotherapy Regimes: Conventional, Normal Hypofractionation, and Fast Forward Hypofractionation

Ruhollah Ghahramani Asl<sup>1,\*</sup>, Pejman Porouhan<sup>1</sup>, Seyed Alireza Javadinia<sup>1</sup>, Aida Omidbakhsh<sup>1</sup>

<sup>1</sup>Department of Radiation Oncology, Vasee Hospital, Sabzevar University of Medical Sciences, Sabzevar, Iran

\* Corresponding Author: Department of Radiation Oncology, Vasee Hospital, Sabzevar University of Medical Sciences, Sabzevar, Iran. Email: gh\_mph@yahoo.com

### Abstract

**Background:** Radiation therapy is commonly used as part of standard adjuvant treatment to improve patient survival in many cases of breast cancer. The present study aims to compare dose-volume histograms of three whole breast radiotherapy regimens: Conventional radiotherapy (CRT), normal hypofractionation (NHRT), and FAST-Forward hypofractionation radiotherapy (FFRT).

**Methods:** This cross-sectional study was conducted at the radiotherapy department of a hospital in Sabzevar, Iran, in 2024. The therapeutic dose for the chest/whole breast and regional lymph nodes was administered using CRT (50 Gy/2 Gy/25 fractions), NHRT (42.56 Gy/2.66 Gy/16 fractions), and FFRT (26 Gy/5.2 Gy/5 fractions) regimens. Cumulative histograms for treatment volumes such as the planning target volume (PTV) and clinical target volume (CTV), as well as volumes related to lung and heart tissue, were calculated and generated using treatment planning system software. These histograms were then compared between the three regimens.

**Results:** The results of this study showed no statistically significant difference in the average scores of PTV V95%, PTV V107-110%, Conformity Index, and Homogeneity Index among the CRT, NHRT, and FFRT treatment regimens (P

> 0.05). However, the average scores of PTV Dmean, lung Vmean, and heart Vmean were significantly higher for CRT and NHRT relative to the FFRT group ( $P < 0.001$ ).

**Conclusions:** The results of the present study indicate that in terms of dose indices, all three treatment regimens are almost similar, but the PTV Dmean and biological effective dose are higher in the CRT treatment regimen. Also, in terms of dose indices such as lung Vmean and heart Vmean delivered to healthy organs, CRT is not superior to the NHRT and FFRT regimens. In some cases, especially NHRT, these regimens can be used interchangeably in unique conditions and crowded government medical centers to provide more treatment services to patients. Considering the economic aspects and lower financial burden on patients and the healthcare system, it may be possible to utilize the NHRT regimen to shorten the radiotherapy duration for the comfort of patients.

**Keywords:** Dose Volume Histogram, Breast Cancer, Radiotherapy

### ■ 4D Respiratory SBRT of Metastatic Small Sized Lung Nodules in Leiomyosarcoma

Faranak Felfeliani<sup>1,\*</sup>, Reza Moghare Abed<sup>1</sup>, Shahram Monadi<sup>1</sup>, Mohsen Saeb<sup>1</sup>, Nikta Monadi<sup>1</sup>

<sup>1</sup>Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran

\* Corresponding Author: Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran. Email: Faranak.felfeliani@yahoo.com

#### Abstract

**Background:** Uterine leiomyosarcoma (ULMS) is a rare disease characterized by high rates of local recurrence and metastasis, with the interval of detection of metastasis varying among patients. The lung is the most common site for metastasis. This study reports a case of ULMS after hysterectomy and the subsequent treatment approach.

**Methods:** A 63-year-old woman with a history of uterine leiomyosarcoma presented with frequent coughs. Restaging positron emission tomography-computed tomography (PET/CT) revealed two active lesions (SUV = 9.6 and 9.8) in the upper lobe of the left lung (1.4 cm) and the lower lobe of the right lung (1.8 cm), respectively. Core needle biopsy confirmed metastatic leiomyosarcoma. The patient underwent stereotactic body radiation therapy (SBRT) for both nodules with a fractionation of 60 Gy in 8 fractions. The CT simulation was performed using a gating respiratory system. Contouring by the physician was performed using the Synovia system, which included the movement of nodules in all directions. Treatment planning was carried out using Monaco version 5.51.11, and treatment was performed using Versa HD (Elekta) with 4D CT image-guided radiation therapy (IGRT) during each session.

**Results:** Follow-up PET/CT six months after treatment showed complete responses of both nodules, with no progression observed until 14 months post-treatment.

**Conclusions:** This case demonstrates that linear accel-

erator-based respiratory gating SBRT is feasible even for small metastatic nodules, providing good local control and limited toxicity in settings lacking real-time gating systems.

**Keywords:** Leiomyosarcoma, Lung, SBRT, Respiratory Gating, PET CT

### ■ Field Size Characteristics in Small Megavoltage Photon Beam Dosimetry

Hadi Keivan<sup>1,\*</sup>, Elahe Tarigati<sup>2</sup>, Reza Maskani<sup>1</sup>

<sup>1</sup>School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran

<sup>2</sup>Iran University of Medical Sciences, Tehran, Iran

\* Corresponding Author: School of Allied Medical Sciences, Shahroud University of Medical Sciences, Shahroud, Iran. Email: hkeivan14@yahoo.com

#### Abstract

**Background:** Small photon beams are increasingly used in modern radiotherapy modalities. However, the dosimetric field size may deviate from the nominal field size in small photon fields. An effective field size (F<sub>Seff</sub>) has been defined to address this issue. The present study aims to examine the suitability of two small sensitive volume ionization chambers and two semiconductor diodes in measuring 6 MV photon beam profiles and to analyze the variations of F<sub>Seff</sub> in smaller fields.

**Methods:** Measurements were conducted using a 6 MV photon beam from a Siemens Artiste linear accelerator. Two ionization chambers (Pinpoint and Semiflex) and two semiconductor detectors (Diode E and Diode P) were used to measure small photon field lateral dose profiles. The F<sub>Seff</sub> was calculated for each nominal field size using the Cranmer-Sargison approach.

**Results:** The uncertainty of the full width at half maximum (FWHM) values derived from the in-plane and cross-plane profiles was below 6% for all detectors, except for the Semiflex chamber in the 1 × 1 cm field size. In small field sizes (less than 3 × 3 cm<sup>2</sup>), larger differences occurred between the dosimetric and nominal field sizes across all detectors. No significant differences between nominal and effective field sizes were observed in a field range of 4 × 4 to 10 × 10 cm<sup>2</sup>.

**Conclusions:** The results indicate that the selection of an appropriate detector is crucial for accurate measurements of small field profiles. The findings support the argument that both the size and composition of detectors affect small field profile measurements. Comparisons with radiochromic film show that a small sensitive volume ion chamber significantly overestimates the F<sub>Seff</sub> in small field sizes, whereas accurate results are obtained with semiconductor diodes.

**Keywords:** Field Size, Radiotherapy, Dosimetry, Photon

### ■ Patient-Specific Quality Assurance in Laryngeal IMRT: Exploring the

## Influence of Thresholds on Gamma Passing Rate Using Gafchromic EBT3 Films

Mohammad Javad Enferadi Aliabad <sup>1,\*</sup>, Mahdie Gholizade <sup>1</sup>, Abolfazl Nikfarjam <sup>1,2</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup>Department of Radiotherapy, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

\* Corresponding Author: Department of Medical Physics, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: enferadiimj@gmail.com

### Abstract

**Background:** Intensity-modulated radiation therapy (IMRT) introduces uncertainties in treatment planning and delivery, necessitating patient-specific quality assurance (PSQA) to ensure dose accuracy. The present study aimed to evaluate the gamma passing rate (GPR) in laryngeal IMRT treatment plans using varying dose difference (DD%), distance-to-agreement (DTA), and low-dose thresholds, along with different normalization methods.

**Methods:** A retrospective analysis was performed on IMRT treatment plans for four laryngeal cancer patients. Plans were created using the Siemens ONCOR linear accelerator and Prowess Panther V5.5. PSQA was conducted with Gafchromic EBT3 films calibrated for doses ranging from 50 to 400 cGy. Gamma analysis evaluated GPR under systematically varied thresholds (DD%: 0.5 - 7%, DTA: 0.5 - 7 mm, low-dose thresholds: 0 - 30%) and normalization methods (global normalization, image reference centroid, and 100 cGy).

**Results:** Higher DD% and DTA thresholds improved GPR. Increasing low-dose thresholds resulted in minor reductions in GPR, with patient one exhibiting the largest decrease (85.48% to 80.14%). Other patients maintained GPR values above 92%. The normalization method significantly influenced results, with global normalization yielding the highest GPR for most patients (81.18 - 95.29%). The reference centroid method yielded the lowest GPR for complex plans (39.19%).

**Conclusions:** Gamma analysis remains essential for PSQA, and parameter variations significantly impact GPR. These findings provide actionable insights into optimizing gamma analysis parameters, particularly for complex laryngeal IMRT plans. Further research with larger sample sizes and varied techniques is recommended to enhance clinical applicability.

**Keywords:** Laryngeal Cancer, IMRT, Gafchromic EBT3 Films

## ■ Impact of CyberKnife Stereotactic Radiosurgery on Ocular Dosimetry in Patients with Brain Tumors

Hamed Zamani <sup>1,2,\*</sup>, Mohsen Saeb <sup>2</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran

\* Corresponding Author: hamed9243483@gmail.com

### Abstract

**Background:** CyberKnife (CK), a sophisticated stereotactic radiosurgery system, has proven to be highly effective in the treatment of brain metastases. This innovative technology provides higher fractional doses of radiation with enhanced precision, potentially leading to improved clinical outcomes. The present study aimed to retrospectively evaluate the ocular dosimetry results during CK treatment for brain tumors.

**Methods:** This study involved 10 patients with various types of brain tumors who received treatment with the CyberKnife system (Accuray Inc., USA) at the Rasa Center in Isfahan Health City between August 1, 2023, and August 1, 2024. For each patient, the volumes of the left and right eye areas within the radiation field were assessed. The minimum and maximum radiation doses received in these target volumes were calculated, and dose-volume histograms (DVHs) were generated to analyze dose distribution.

**Results:** Among the 10 patients, there were 5 females and 5 males, with an average age of  $50.9 \pm 2.47$  years. The mean volume of the treated eye area was  $16.11 \pm 1.05$  cm<sup>3</sup>. The average radiation dose delivered was 23.98 Gy (ranging from 13 to 35 Gy, with 5 - 10 Gy per fraction across 1 to 5 fractions). The doses received in the eye area were as follows: Minimum dose ( $0.123 \pm 0.103$  Gy), mean dose ( $0.882 \pm 0.912$  Gy), and maximum dose ( $3.40 \pm 2.11$  Gy).

**Conclusions:** CyberKnife radiosurgery exhibits remarkable precision in the treatment of brain metastases, resulting in minimal radiation exposure to ocular structures. The study highlighted a notably low mean dose to eye tissue of  $0.882 \pm 0.912$  Gy, emphasizing the technology's capability to effectively target tumors while safeguarding sensitive ocular regions. This advanced technique not only offers high local control rates and improved survival outcomes but also reduces treatment-related complications. By facilitating precise and dynamic radiation delivery with minimal invasiveness, CyberKnife represents a significant advancement in stereotactic radiosurgery for the management of complex brain metastases.

**Keywords:** CyberKnife, Stereotactic Radiosurgery, Brain Metastases, Ocular Dosimetry, Eye Protection

## ■ Efficacy of CyberKnife Stereotactic Radiosurgery in the Treatment of Brain Metastases: A Retrospective Analysis

Hamed Zamani <sup>1,2,\*</sup>, Mohsen Saeb <sup>2</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Rasa Imaging and Therapy Center, Isfahan Healthcare City, Isfahan, Iran

\* Corresponding Author: hamed9243483@gmail.com

### Abstract

**Background:** CyberKnife, a cutting-edge stereotactic radiosurgery system, has demonstrated considerable effectiveness in the management of brain metastases. This innovative technology administers higher fractional doses of radiation with enhanced precision, potentially leading to improved clinical outcomes. The present study aimed to conduct a retrospective analysis of the clinical outcomes for patients with brain tumors treated using CyberKnife.

**Methods:** This study involved 10 patients diagnosed with various brain tumors, all treated with the CyberKnife system (Accuray Inc., USA) at the Rasa Center in Isfahan Health City from August 1, 2023, to August 1, 2024. Treatment planning was facilitated by the Precision Accuray Treatment Planning System (TPS) (CyberKnife Medical System, Version 2.0.1.1, USA) specifically for brain metastases. For each patient, the planning target volume (PTV), clinical target volume (CTV), and gross tumor volume (GTV) were established. The minimum, maximum, and average radiation doses received in these target volumes were calculated, and dose-volume histograms (DVHs) were generated to evaluate dose distribution.

**Results:** Among the 10 patients, there were 5 females and 5 males, with a mean age of  $50.9 \pm 2.47$  years. A total of 18 lesions were treated, with an average lesion size of 19.88 cm<sup>3</sup>. The mean radiation dose administered was 23.98 Gy (ranging from 13 to 35 Gy, with 5 - 10 Gy per fraction across 1 to 5 fractions). The doses received in the target volumes were as follows: Minimum dose ( $17.98 \pm 5.44$  Gy); mean dose ( $26.37 \pm 6.15$  Gy); and maximum dose ( $30.32 \pm 7.39$  Gy). **Conclusions:** The use of CyberKnife radiosurgery, which employs higher doses per fraction, has shown excellent clinical outcomes in the treatment of brain metastases. This study indicates that CyberKnife is a viable and effective treatment option, yielding high local control rates and enhanced survival outcomes. Its capacity to deliver precise, high-dose radiation while minimizing damage to surrounding healthy brain tissue makes it a valuable tool for managing multiple brain metastases, particularly in cases where conventional treatments may be less effective.

**Keywords:** CyberKnife, Stereotactic Radiosurgery, Brain Metastases, Clinical Outcomes, PTV, CTV

### ■ Radiomics Based Predictive Modeling of Rectal Toxicity in Prostate Cancer Patients Undergoing Radiotherapy: CT and MRI Comparison

Hossein Hassaninejad <sup>1,\*</sup>, Mohammad Bagher Tavakkoli <sup>1</sup>, Iraj Abedi <sup>1</sup>, Hamid Abdollahi <sup>1</sup>, Alireza Amouheidari <sup>1</sup>, Mohammad Hossein Shakeri <sup>1</sup>

<sup>1</sup>Department of Radiology, Faculty of Paramedical, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

\* Corresponding Author: Department of Radiology, Faculty of Paramedical, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. Email: h.hassaninejad68@rums.ac.ir

#### Abstract

**Background:** Rectal toxicity is a common side effect of radiotherapy in prostate cancer patients. Radiomics offers a non-invasive and cost-effective method to predict radiation toxicity, overcoming the limitations of traditional methods. By analyzing radiomic features from computed tomography (CT) and magnetic resonance (MR) images and applying machine learning, the present study aims to predict rectal radiation toxicity with reliable performance.

**Methods:** In a prospective trial, 70 men with confirmed prostate cancer undergoing three-dimensional conformal radiotherapy (3DCRT) were studied. Radiomic features were extracted from rectal wall CT and MR images. The least absolute shrinkage and selection operator (LASSO) method was used for feature selection, and classifiers such as random forest, decision tree, logistic regression, and K-nearest neighbors were employed to build predictive models. These models incorporated radiomic, dosimetry, and clinical data alone or in combination. Performance was evaluated using the area under the receiver operating characteristic curve (AUC-ROC), accuracy, sensitivity, and specificity.

**Results:** The best outcomes were achieved by the radiomic features of MR images in conjunction with clinical and dosimetry data, with a mean AUC of 0.79, accuracy of 77.75%, specificity of 82.15%, and sensitivity of 67%.

**Conclusions:** This study demonstrated that the radiomic features of MR images before treatment perform better than those of CT for the development of rectal radiation toxicity prediction models. Furthermore, when the radiomic features of images are combined with the clinical and dosimetry parameters of patients, the performance of predictive models improves.

**Keywords:** Rectal Toxicity, Radiotherapy, Prostate Cancer, Radiomic Features of MR Images

### ■ Comparison Prediction Models of Bladder Toxicity Based on Radiomic Features of CT and MRI in Patients with Prostate Cancer Undergoing Radiotherapy

Hossein Hassaninejad <sup>1,\*</sup>, Mohammad Bagher Tavakkoli <sup>1</sup>, Iraj Abedi <sup>1</sup>, Hamid Abdollahi <sup>1</sup>, Alireza Amouheidari <sup>1</sup>, Rasool Azmoonfar <sup>1</sup>, Korosh Saber <sup>1</sup>

<sup>1</sup>Department of Radiology, Faculty of Paramedical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

\* Corresponding Author: Department of Radiology, Faculty of Paramedical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. Email: h.hassaninejad68@rums.ac.ir

#### Abstract

**Background:** Bladder radiation toxicity is a side effect of prostate cancer radiation therapy. Radiomics, a non-invasive imaging method, can predict radiation toxicity in healthy tissue. The present study utilized computed tomography (CT) and magnetic resonance imaging (MRI) radiomic features of the bladder wall before treatment to

develop predictive models for bladder toxicity. This is the first study comparing the predictive power of CT and MRI radiomics for bladder radiation toxicity.

**Methods:** This study involved 70 prostate cancer patients eligible for radiation therapy. Computed tomography and MRI images of the bladder wall were used to extract radiomic features. The least absolute shrinkage and selection operator (LASSO) was applied for feature selection, and models were developed using algorithms such as random forest, decision tree, logistic regression, and K-nearest neighbors, based on radiomic, dosimetry, and clinical data. The predictive power of the models was analyzed using the area under the receiver operating characteristic curve (AUC) and accuracy.

**Results:** The random forest and logistic regression models based on the radiomic features of MRI and clinical/dosimetry parameters achieved the highest performance in predicting bladder radiation toxicity, with an AUC of 0.95 and 0.93, and an accuracy of 86% for both models.

**Conclusions:** This study demonstrated that MRI radiomic features of the bladder wall before treatment could be used to predict bladder radiotoxicity. Furthermore, MRI is superior to CT in predicting bladder radiotoxicity. Additionally, the performance of predictive models improved when combining radiomic, clinical, and dosimetry characteristics.

**Keywords:** Bladder Toxicity, Radiomic Features, Radiotherapy.

## ■ Comparison of Dose Enhancement Among Bismuth, Gold, and Platinum Nanoparticles with HDR Sources in Brachytherapy: A Monte Carlo Study

Sajjad Aghasizadeh <sup>1,\*</sup>, Nazanin Oroskhani <sup>2</sup>

<sup>1</sup>Department of Medical Physics, Kashan University of Medical Sciences, Kashan, Iran

<sup>2</sup>Department of Medical Physics, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Medical Physics, Kashan University of Medical Sciences, Kashan, Iran. Email: sajjad.aghaji.medicalphysics@gmail.com

### Abstract

**Background:** The present study aimed to determine the dose enhancement factor achieved by bismuth, gold, and platinum nanoparticles in brachytherapy. For this purpose, the Geant4 Monte Carlo code was utilized to simulate three brachytherapy sources: Yb-169, Co-60, and Ir-192. The obtained values of dose rate constants and radial dose functions were compared with corresponding published values for these sources to verify the accuracy of our simulations.

**Methods:** A cubic soft tissue phantom with dimensions of 30 cm was simulated to investigate the dose enhancement factor. Bismuth, gold, and platinum nanoparticles, each with a diameter of 50 nm and a concentration of 18 mg/mL, were then separately simulated within a tumor

within a volume of 1 × 1 × 1 cm<sup>3</sup> cubic.

**Results:** The findings indicated that the dose enhancement within the tumor in the presence of bismuth, gold, and platinum nanoparticles using the Co-60 source was 0.96%, 0.95%, and 0.94%, respectively. Additionally, for the Ir-192 source, these values were reported as 3.31%, 3.27%, and 3.20%, respectively, and for the Yb-169 source, the dose enhancements were 37.1%, 36%, and 34.5%.

**Conclusions:** Based on the simulation results, it can be concluded that bismuth nanoparticles provide a greater dose enhancement compared to gold and platinum. The highest dose enhancement occurs when using low-energy sources such as Yb-169. Therefore, the clinical use of these nanoparticles is recommended for dose enhancement in brachytherapy.

**Keywords:** Bismuth Nanoparticles, Gold, Platinum, HDR, Brachytherapy

## ■ Advance Cervical Cancer Radiotherapy: A Systematic Comparison of Proton Therapy and IMRT Dosimetric Outcomes

Mohammad Javad Enferadi Aliabad <sup>1,\*</sup>, Zeinab Sadeghian <sup>1</sup>, Javad Biabani Ardakani <sup>2</sup>, Abolfazl Nickfarjam <sup>1</sup>

<sup>1</sup>Department of Medical Physics, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup>Biotechnology Research Center, Yazd Reproductive Sciences Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

\* *Corresponding Author:* Department of Medical Physics, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: enferadiimj@gmail.com

### Abstract

**Background:** Cervical cancer remains a significant global health concern, with advanced radiation therapies such as intensity-modulated radiation therapy (IMRT) and proton therapy demonstrating potential to optimize treatment by sparing healthy tissues.

**Methods:** A systematic review was conducted to compare the dosimetric outcomes of IMRT and proton therapy in cervical cancer treatment. Relevant studies published between 2013 and 2023 were retrieved from PubMed, Scopus, Cochrane, and Embase. The search strategy included Boolean operators and keywords such as "IMRT", "proton therapy" and "dosimetric outcomes". Studies reporting specific dose-volume histogram (DVH) metrics for organs at risk (OARs) were included. Data were extracted independently by two reviewers, focusing on parameters such as mean dose (D<sub>mean</sub>), maximum dose (D<sub>max</sub>), and dose-volume thresholds (e.g., V<sub>30</sub>, V<sub>40</sub>).

**Results:** Proton therapy, particularly intensity-modulated proton therapy (IMPT), achieved superior sparing of OARs compared to IMRT. For the bladder, IMPT reduced D<sub>mean</sub> by 15 - 38% (23.4 - 37.5 Gy for IMPT vs. 34.5 - 48.5 Gy for IMRT) and V<sub>45</sub> by 12.1% (IMPT: 31.9%, IMRT: 44%). Rectal sparing was significant, with D<sub>mean</sub> reduced by 9 - 36% (IMPT: 24.3 - 38.3 Gy, IMRT: 33.7 - 45.9 Gy) and V<sub>30</sub> lowered

by 6 - 20%. The IMPT also reduced femoral head Dmean by 6 - 58%, preserving bone health, and minimized bone marrow exposure, with Dmean dropping from 33.1 Gy (IMRT) to 19.4 Gy (IMPT-BMS).

**Conclusions:** Proton therapy provides superior dosimetric outcomes, reducing toxicity risks and improving treatment feasibility for cervical cancer patients. These findings highlight its potential to enhance clinical outcomes in radiation oncology.

**Keywords:** Proton Therapy, Radiotherapy, IMPT, Cervical Cancer

## ■ The Effect of Acupressure on Sleep Quality in Patients with Leukemia: A Single-Center, Randomized Controlled Trial

Hanieh Molaei<sup>1,\*</sup>, Rasoul Goli<sup>2</sup>, Navid Faraji<sup>2</sup>, Niloofar Najafali Dizaji<sup>2</sup>, Mojde Bagheri<sup>3</sup>, Sina Shakorzadeh<sup>4</sup>, Amireh Hassanpour<sup>2</sup>, Fatemeh Imanzadeh<sup>4</sup>, Raheleh Lameei<sup>2</sup>

<sup>1</sup>Department of Nursing, Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Urmia University of Medical Sciences, Urmia, Iran

<sup>3</sup>Department of Medicine, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup>Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Islamic Azad University, Urmia Branch, Urmia, Iran

\* *Corresponding Author:* Department of Nursing, Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: haniehmolaei991373@gmail.com

### Abstract

**Background:** Sleep disturbances are a common problem among patients with leukemia, adversely impacting their quality of life and overall well-being. Acupressure has been suggested as a non-pharmacological intervention for improving sleep quality. The present study aimed to determine the effect of acupressure on sleep quality in patients with leukemia.

**Methods:** This single-blinded randomized controlled trial employed a pretest-posttest design, with a total of 68 participants randomly allocated into two groups: An intervention group receiving acupressure therapy on the SP6 point for 10 minutes twice a day, in the morning and evening, and a control group receiving routine care. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality at baseline and after a 4-week intervention period. Data were evaluated using coded research units and analyzed with SPSS version 25, employing chi-square, Fisher, and t-tests.

**Results:** The results revealed a significant improvement in sleep quality among participants in the intervention group compared to the control group after acupressure therapy on the SP6 point ( $P < 0.001$ ). The mean PSQI score decreased from  $16.39 \pm 1.32$  to  $12.27 \pm 1.84$  in the intervention group, whereas it only decreased from  $16.78 \pm 1.38$  to  $16.21 \pm 1.40$  in the control group.

**Conclusions:** Acupressure appears to be an effective non-

pharmacological intervention for improving sleep quality in patients with leukemia. The findings of this study could contribute to developing comprehensive supportive care strategies in the management of leukemia, ultimately enhancing the overall well-being and quality of life of these patients.

**Keywords:** Leukemia, Acupressure, Nursing

## ■ The Impact of Laughter Therapy on the Quality of Life of Cancer Patients: A Systematic Review

Marzieh Barahooei Noori<sup>1,\*</sup>

<sup>1</sup>Department of Community Health, Faculty of Nursing and Midwifery, Zahedan University of Medical Sciences, Zahedan, Iran

\* *Corresponding Author:* Department of Community Health, Faculty of Nursing and Midwifery, Zahedan University of Medical Sciences, Zahedan, Iran. Email: barahooei@gmail.com

### Abstract

**Background:** The quality of life in cancer patients is significantly affected by the physical and psychological side effects of treatment. Laughter therapy, a form of cognitive-behavioral therapy, enhances physical, psychological, and social well-being, ultimately improving quality of life. Given the importance of quality of life in these patients, this study aims to review the evidence and assess the impact of laughter therapy on the quality of life of cancer patients.

**Methods:** In this systematic review, an extensive search was conducted using keywords related to laughter therapy, quality of life, and cancer in international databases such as Scopus, Web of Science Core Collection, PubMed/Medline, and the search engine Google Scholar, as well as national databases SID, Magiran, and Irandoc. Inclusion criteria included free access to full-text articles and publication in either Persian or English. Review studies, letters to the editor, and conference papers were excluded. No time limitations were applied. A total of 60 studies were identified in the initial search. After removing duplicates and conducting critical appraisal with relevant tools, 5 studies were ultimately analyzed. Ethical considerations regarding bias in assignment, extraction, analysis, and classification of evidence were adhered to, and the abstract was reported according to PRISMA guidelines.

**Results:** Most of the studies conducted were randomized clinical trials, with a higher concentration in Asian countries. The review indicated that implementing a structured laughter therapy intervention in a hospital setting improves health-related quality of life for cancer patients. This intervention enhances emotional functioning and reduces fatigue, pain, and sleep disturbances. Laughter contributes to the improvement of stress, depression, and emotional well-being, and can serve as a complementary treatment with minimal side effects for cancer patients. Furthermore, laughter therapy, as a nursing intervention, leads to a reduction in perceived stress

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and an increase in quality of life.

**Conclusions:** Overall, this study demonstrated that laughter therapy is effective in enhancing the quality of life for cancer patients. Given the importance of this topic, it is essential for nursing managers in oncology departments to utilize this therapeutic approach, which is non-invasive and cost-free, as a complementary treatment for cancer patients.

**Keywords:** Laughter Therapy, Quality of Life, Cancer

## ■ Evaluation of the Role of the Clinical Nurse Specialist in Cancer Care

Maryam Sodmand <sup>1,\*</sup>

<sup>1</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: maryamsodmand71@gmail.com

### Abstract

**Background:** Clinical nurse specialists (CNS) play a pivotal role in providing complex and specialized care to cancer patients, given their advanced education and clinical skills. This comprehensive review aimed to assess the role of CNS in improving treatment outcomes, patient quality of life, and healthcare system efficiency. The study evaluates the multifaceted role of clinical nurse specialists in cancer care, focusing on their impact on patient outcomes, healthcare system efficiency, and overall care quality. The findings seek to underscore the importance of CNS as an integral part of the multidisciplinary cancer care team.

**Methods:** A narrative review was conducted by searching reputable databases, including PubMed, CINAHL, and Cochrane Library. The following search keywords and phrases were used: "Clinical Nurse Specialist", "cancer care", "patient outcomes", "quality of life", "symptom management" and "healthcare efficiency". Boolean operators (AND, OR) were applied to refine the search strategy. The inclusion criteria for selecting studies were: Peer-reviewed articles published in English between 2010 and 2023, studies focusing on the role of CNS in cancer care and research analyzing patient outcomes, healthcare system efficiency, or multidisciplinary care contributions.

### **Results:**

Categories	Subcategories	Details
Patient outcomes	Improved management of symptoms (e.g., pain, fatigue, nausea)	Enhanced patient comfort and ability to participate in daily activities
	Increased adherence to treatment plans through tailored education and support	Improved treatment efficacy and reduced risk of complications

	Reduction in emotional distress and enhanced coping mechanisms	Improved mental health and overall quality of life
	Greater patient satisfaction with care delivery	Higher trust in the healthcare team and better patient-provider relationships
Health-care efficiency	Decreased hospital length of stay due to effective care planning	Reduced healthcare costs and resource utilization
	Lower readmission rates through proactive symptom management and follow-ups	Improved healthcare system efficiency and patient outcomes
	Enhanced communication and care coordination among multidisciplinary teams	Seamless transitions of care and minimized care fragmentation
CNS contributions	Development of personalized care plans tailored to individual needs and conditions	Addressed unique patient challenges, leading to better outcomes
	Delivery of structured patient education on treatment processes, side effects, and self-management	Empowered patients to manage their conditions confidently and independently
	Leadership in care coordination, acting as a bridge between providers and patients	Improved teamwork and ensured that all aspects of care were addressed comprehensively
	Provision of emotional and psychological support for patients and families coping with cancer	Enhanced emotional well-being and reduced caregiver burden
Professional development	Enhanced CNS knowledge and expertise through specialized oncology training	Greater competence in managing complex cancer care scenarios
	Promotion of evidence-based practice through research and continuous education	Improved integration of the latest advancements in patient care strategies
	Mentorship and leadership roles within the healthcare team	Strengthened team performance and enhanced professional growth for junior staff

**Conclusions:** The findings suggest that healthcare systems should prioritize investment in the development and expansion of Clinical Nurse Specialist (CNS) roles, as this can lead to higher quality care, improved patient experiences, and more efficient healthcare delivery. Future studies are recommended to further explore CNS effectiveness across diverse cancer populations and settings, as well as their impact on long-term survivorship care and palliative support.

**Keywords:** Clinical Care Specialist, Healthcare, Cancer

### ■ The Effect of Topical Aloe Vera on Radiotherapy-Induced Dermatitis: A Systematic Review

Mohammad Chahkandi <sup>1,\*</sup>, Farzaneh Pardehshenas <sup>1</sup>

<sup>1</sup>Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

\* *Corresponding Author:* Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran. Email: chahkandim4022@mums.ac.ir

#### Abstract

**Background:** Radiation-induced dermatitis (RID) is a prevalent side effect of radiation therapy, with up to 90% of patients experiencing skin reactions during treatment. These reactions compromise treatment continuity, patient health, and quality of life. Various topical agents, including Aloe vera (AV), have been investigated for their efficacy in managing RID. This systematic review evaluates evidence on the effectiveness of Aloe vera-based products in preventing and treating RID.

**Methods and Materials:** This systematic review adhered to PRISMA 2020 guidelines. A comprehensive search was conducted in PubMed, Cochrane, CINAHL, Magiran, SID databases, and the Google Scholar search engine for articles published between 2014 and 2024. Inclusion criteria encompassed studies focusing on the effects of topical Aloe vera on radiodermatitis. Exclusion criteria involved deviations from these parameters, utilizing unsuitable study types or publications outside the specified period. The initial search yielded 43 articles, of which 9 met the inclusion criteria and were analyzed.

**Results:** The findings from 9 studies revealed mixed results regarding the efficacy of Aloe vera for RID management. Some studies demonstrated that Aloe vera gel or cream significantly reduced the severity of moderate to severe RID and instances of moist desquamation, particularly in patients with head and neck cancers. For example, higher concentrations of Aloe vera (75%) showed better outcomes in reducing acute dermatitis than lower

concentrations (10%). Similarly, combining Aloe vera with other agents, such as daikon gel, showed promising results in mitigating RID severity. However, one randomized trial reported no significant effect of Aloe vera on the prevalence or severity of RID. Despite these positive findings, the prophylactic efficacy of Aloe vera for preventing RID remains inconclusive.

**Conclusions:** While the use of Aloe vera gel or cream for the prevention of radiodermatitis remains uncertain, the topical application of Aloe vera has often been shown to delay the onset of radiodermatitis, accelerate the healing process, and reduce moist desquamation. It is recommended for patients undergoing radiotherapy.

**Keywords:** Radiodermatitis, Aloe Vera, Radiotherapy, Radiation-Induced Dermatitis

### ■ The Role of Nurses in Managing Lymphedema in Cancer Patients

Fatemeh Mohamadian <sup>1,\*</sup>

<sup>1</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: fatemehmohamadian7819@gmail.com

#### Abstract

**Background:** Lymphedema is a chronic, debilitating condition that arises from a disruption of the lymphatic system, often occurring following cancer treatments, especially surgery in the chest and pelvic regions. It can lead to swelling, impaired limb function, and psychological distress, significantly affecting patients' quality of life. Nurses play a pivotal role in managing lymphedema, contributing significantly to patient care and improving outcomes. The present study aims to highlight the critical role of nurses in the management of lymphedema in cancer patients by exploring their contributions to early detection, patient education, therapeutic interventions, and psychological support. The findings emphasize the importance of a multidisciplinary approach in enhancing patient outcomes and quality of life.

**Methods and Materials:** A narrative review of the literature was conducted by searching Google Scholar, PubMed, and Scopus databases for articles published between 2014 and 2024. Keywords such as "nursing", "lymphedema", "cancer" and "management" were used to identify relevant studies. A total of 20 articles were included in the analysis, focusing on nurse-led interventions and their impact on lymphedema management.

**Results:**

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Category	Subcategory	Details
Patient education	Patients about the causes, symptoms, and management strategies for lymphedema. Education includes information on lifestyle modifications, such as weight management, avoiding tight clothing, and proper skin care to prevent infection. Nurses also teach self-monitoring techniques, helping patients recognize early signs of lymphedema and take timely action	Improved self-management: Patients are better equipped to manage their condition independently
		Increased patient compliance: Educated patients are more likely to adhere to treatment plans and lifestyle changes
		Reduced swelling: Proper care and awareness can prevent further fluid accumulation and reduce the severity of swelling
Prevention strategies	Compression bandaging is a cornerstone of lymphedema management. Nurses train patients in the proper technique for applying and wearing bandages, which helps to reduce swelling and promote the reabsorption of lymphatic fluid. Bandaging techniques include multi-layer compression bandages and gradient compression	Reduction in limb swelling: Compression bandaging helps prevent further lymphatic fluid buildup, reducing swelling in affected areas
		Prevention of tissue fibrosis: Continuous compression prevents the development of thick, fibrous tissue that can result from prolonged swelling
		Improved limb function: As swelling decreases, mobility and strength in the affected limb improve
Management strategies	Manual lymphatic drainage (MLD) and other massage techniques are commonly used by nurses to enhance lymph flow and reduce swelling. The MLD is a specialized massage technique designed to stimulate the lymphatic system and encourage fluid drainage. Nurses often teach patients self-massage techniques for ongoing management	Enhanced lymphatic circulation: MLD helps to stimulate the flow of lymph and reduce the build-up of fluid in tissues
		Improved limb mobility: The massage promotes better function and flexibility in affected limbs
		Reduced pain and discomfort: Massage therapy alleviates the discomfort and heaviness caused by swelling, enhancing patients' comfort and quality of life

Ongoing assessment and follow-up	Nurses conduct regular assessments to monitor the progression of lymphedema and to detect any complications, such as infection, fibrosis, or new areas of swelling. Follow-up visits allow nurses to adjust treatment plans, assess the effectiveness of interventions, and provide additional education or support	Prevention of complications: Regular monitoring ensures that early signs of infection or fibrosis are detected, preventing further tissue damage
		Personalized care: Nurses can adjust treatment plans based on the patient's current condition, ensuring individualized care
		Better long-term outcomes: Continued assessment helps maintain the effectiveness of the management plan, leading to better long-term control of the condition

**Conclusions:** Incorporating comprehensive, nurse-led care into lymphedema management protocols is essential for improving patient outcomes, reducing complications, and increasing patient satisfaction. The contributions of nurses to this area of cancer care are invaluable, underscoring the need for specialized training and continuous support for healthcare providers involved in lymphedema management.

*Keywords:* Lymphedema, Nursing, Specialized Training

## ■ The Relationship Between Awareness of Illness and Hope for Life in Cancer Patients

Atousa Afsari <sup>1, \*</sup>, Reyhane Ghaleghovand <sup>1</sup>, Hadise Katebi <sup>1</sup>

<sup>1</sup>Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran

\* *Corresponding Author:* Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran. Email: afsariatousa1@gmail.com

### Abstract

**Background:** The field of care and treatment for cancer patients is one of the most challenging areas in medical care, presenting numerous difficulties. One of the ethical challenges in the care of these patients is informing them about their diagnosis, with concerns that awareness of their condition may diminish their hope. The aim of this review study is to investigate the relationship between awareness of illness and hope for life in cancer patients.

**Methods:** This systematic review was conducted using search engines such as MAGIRAN, IRANDOC, SCOPUS, Google Scholar, and MEDLINE from 2010 to the present.

**Results:** Based on the studies conducted, awareness of one's diagnosis does not have a negative impact on the level of hope among cancer patients; in fact, those who are aware tend to have greater hope than those who are unaware of their condition. Furthermore, patients express a desire to be informed about the stages of their illness, potential for improvement, various treatment options, personal care, and sexual health issues.

**Conclusions:** Considering that awareness of illness does not diminish hope in cancer patients, this underscores the necessity for greater attention and training for healthcare providers — including physicians and nurses — regarding the importance of effective communication and how to convey essential information about the illness. This can positively influence care dimensions, enhance quality of life, and increase patients' motivation and cooperation in their treatment and care.

**Keywords:** Awareness, Hope for Life, Cancer Patient

### ■ A Systematic Review of the Impact of Virtual Reality on Pain and Anxiety Levels in Cancer Patients

Seyedeh Atoosa Ramezani <sup>1,\*</sup>, Ali Tamimi <sup>2</sup>

<sup>1</sup>Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran

\* *Corresponding Author:* Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran. Email: Atoosaramezani8090@gmail.com

#### Abstract

**Background:** Virtual reality (VR) has emerged as a novel technology in pain management, functioning as a distraction technique that immerses patients in real-life sensations through hardware and software. Cancer patients often face chronic pain and side effects resulting from chemotherapy and radiation therapy. This review aims to analyze previous studies to assess the impact of virtual reality on pain and anxiety levels in cancer patients.

**Methods:** A systematic review was conducted following the PRISMA guidelines. The research utilized keywords such as "virtual reality", "cancer patients", "cancer pain" and "anxiety". The databases searched for articles included PubMed, Scopus, and Google Scholar. The inclusion criteria encompassed VR interventions conducted on cancer patients from 2015 to 2024, while the exclusion criteria involved studies that lacked usable quantitative data for analysis or were unrelated to the topic. Data extraction and evaluation were performed independently by two reviewers to prevent bias and ensure objectivity.

**Results:** Out of the initial 500 articles, 30 studies met the inclusion criteria. The findings indicated that VR-based interventions significantly reduced pain and anxiety levels. Most respondents found the use of VR to be a beneficial adjunct therapy for managing chronic cancer

pain, with the content and duration of the intervention affecting its effectiveness. Short-term interventions (lasting less than six weeks) were effective in alleviating pain, while game-focused activities, watching films, enjoying scenic views, and health-related educational content were beneficial in reducing patients' anxiety and alleviating negative psychological symptoms associated with the illness.

**Conclusions:** Overall, virtual reality has gained attention as a complementary tool in pain treatment, and physicians may consider VR technology as an adjunct intervention for managing pain and anxiety. However, there is a need for high-quality methodological studies to determine best practices for use and to evaluate the long-term effects.

**Keywords:** Virtual Reality, Cancer Patients, Cancer Pain, Anxiety

### ■ A Systematic Review of the Impact of Clown Therapy on Pain and Anxiety Reduction in Children with Cancer

Seyedeh Atoosa Ramezani <sup>1,\*</sup>, Alireza Momtaz Hamginy <sup>1</sup>, Gholamreza Akbari <sup>1</sup>, Ali Tamimi <sup>1</sup>

<sup>1</sup>Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran

\* *Corresponding Author:* Student Research Committee, Abadan University of Medical Sciences, Abadan, Iran. Email: Atoosaramezani8090@gmail.com

#### Abstract

**Background:** Clown therapy is an innovative approach in which trained professionals use entertaining techniques and humor to create a joyful and positive environment for children with cancer. This, in turn, can help alleviate feelings of fear and anxiety associated with medical treatments. The present review aimed to analyze previous studies and determine the efficacy of clown therapy in reducing pain and anxiety among children with cancer.

**Search Strategy:** A systematic review was conducted following the PRISMA guidelines. This research utilized keywords such as "clown therapy", "cancer patients", "cancer pain" and "anxiety". The databases used for article searches included PubMed, Scopus, and Google Scholar. The inclusion criteria comprised clown therapy interventions conducted on children with cancer between 2015 and 2024, while the exclusion criteria encompassed studies that lacked usable quantitative data for analysis and articles unrelated to the topic. Data extraction and evaluation were performed independently by two reviewers to minimize bias.

**Results:** Out of the 200 initial articles reviewed, 20 studies met the inclusion criteria. According to the results, clown therapy is effective in alleviating pain and anxiety in children undergoing chemotherapy. This method helps children feel more comfortable by fostering social interactions and stimulating laughter and joy, leading to reduced cortisol levels and increased endorphin production. Consequently, it helps to distance them from the

stresses associated with their illnesses and treatments. Our findings clearly support the benefits of medical clowning programs in enhancing the short-term emotional well-being of pediatric patients.

**Conclusions:** Given the positive impact of clown therapy on improving the psychological and emotional well-being of children, these interventions should be regarded as effective complements to traditional medical treatments. They transform stressful hospital environments into more supportive spaces for children. However, additional research is needed to strengthen this evidence and enhance the implementation of the intervention.

**Keywords:** Clown Therapy, Cancer Patients, Cancer Pain, Anxiety

### ■ The Role of Artificial Intelligence in Providing Treatment and Care Services for Cancer Patients

Atousa Afsari <sup>1,\*</sup>, Reyhane Ghaleghovand <sup>1</sup>, Hadise Katebi <sup>1</sup>

<sup>1</sup>Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran

\* *Corresponding Author:* Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran. Email: afsariatousa1@gmail.com

#### Abstract

**Background:** Artificial intelligence (AI), as one of the advanced new technologies, is rapidly transforming various aspects of the medical field, particularly in oncology. Given the increasing prevalence of cancer and the need for complex and multifaceted care, AI technologies can enhance decision-making processes and reduce human error. The present review study aimed to examine the role of AI in providing treatment and care services for cancer patients.

**Methods:** This systematic review was conducted using search engines such as MAGIRAN, IRANDOC, Google Scholar, SCOPUS, and PubMed from 2019 to the present.

**Results:** Results from multiple studies indicate that the application of AI in providing treatment services can facilitate tasks such as predicting tumor pathology, gene therapy, diagnosing and predicting treatment responses, evaluating new anomalies, drug discovery, and more. Additionally, AI can be utilized in certain tasks such as processing patient data, documentation, and providing support in clinical decision-making to enhance nurses' care for patients.

**Conclusions:** Considering the high potential of AI to improve the quality of treatment and care services for cancer patients, it is anticipated that more specialized training for physicians and nurses will be necessary to increase their knowledge and application of this technology across various therapeutic and caregiving domains.

**Keywords:** Artificial Intelligence, Treatment, Care, Cancer

### ■ Prevalence of Health Anxiety and Hypochondriasis in Cancer Care Workers

Alireza Soltani <sup>1,\*</sup>, Mohammadamin Abdi <sup>2</sup>, Shaghayegh Haghi <sup>3</sup>

<sup>1</sup>Kerman Comprehensive Radiation Oncology Center, Afzalipour Hospital, Kerman, Iran

<sup>2</sup>Department of Psychiatry, Kerman University of Medical Sciences, Iran

<sup>3</sup>Department of Occupational Therapy, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Kerman Comprehensive Radiation Oncology Center, Afzalipour Hospital, Kerman, Iran. Email: Alirezasoltani1995@gmail.com

#### Abstract

**Background:** Given the emotional demands on the cancer care team, understanding the prevalence of health anxiety in this population is crucial for ensuring both caregiver well-being and patient care quality. This study aims to investigate the relationship between working with cancer patients and the manifestation of hypochondriasis among healthcare professionals.

**Methods:** This cross-sectional study involved 49 participants, utilizing the health anxiety inventory (HAI-18) questionnaire to assess levels of health anxiety. Demographic data, including age, gender, marital status, level of education, and cancer history in first-degree relatives, were also collected for comprehensive analysis. Data analysis employed independent samples t-tests for age and Pearson's chi-square tests for other demographic factors.

**Results:** The findings reveal that 16.3% of cancer care workers exhibit pathological health anxiety disorder, higher than the 6% prevalence found in the general population, with a P-value of 0.0096, indicating a statistically significant difference. Notably, no significant relationships were identified between health anxiety and demographic variables or cancer history in first-degree relatives.

**Conclusions:** These results suggest that cancer care workers are at a heightened risk for developing health anxiety compared to the general public. The implications of this finding are critical; it underscores the need for increased awareness and intervention strategies to address mental health concerns within this occupational group. The elevated prevalence of health anxiety may adversely affect the quality of care provided to cancer patients, highlighting the necessity for supportive measures aimed at mitigating psychological distress among healthcare providers. This study contributes valuable insights into the mental health challenges faced by cancer care workers and calls for further research and policy attention to enhance their well-being and professional efficacy.

**Keywords:** Hypochondriasis, Cancer Care Workers, Nurses, Anxiety

## ■ The Role of Nurses in Managing Adverse Effects of Targeted Therapy in Cancer

Somayeh Sayadinejad<sup>1,\*</sup>

<sup>1</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: som.nur61@gmail.com

### Abstract

**Background:** Targeted therapy is a novel approach in cancer treatment. Although it reduces side effects compared to traditional methods, it can still induce adverse effects that necessitate specialized nursing care. This study aimed to investigate the role of nurses in identifying, predicting, and managing adverse effects associated with targeted therapy in cancer patients.

**Method:** This narrative review was conducted by searching for articles using keywords such as “nursing”, “adverse effects”, “cancer”, “management” and “target therapy” through Google Scholar, PubMed, and Scopus databases from 2014 to 2024. A total of 18 articles were retrieved and analyzed to assess the nurse’s role at various stages of treatment, including patient education, continuous assessment of the patient’s condition, early detection of adverse effects, and providing supportive care.

**Results:** Patient education, continuous assessment of the patient’s condition, early detection of adverse effects, and providing supportive care are four core components of nursing care. By providing necessary education to patients, assisting them in identifying early signs of adverse effects, and collaborating with the treatment team, nurses can significantly improve patients’ quality of life and reduce adverse effects. Furthermore, nurses can effectively manage adverse effects by utilizing standardized assessment tools and evidence-based nursing interventions.

**Conclusions:** Nurses, as integral members of the cancer care team, play a pivotal role in managing the adverse effects of targeted therapy. Given the complexity of this treatment and the significance of nursing care, it is essential to enhance nurses’ knowledge and skills in this area. Additionally, developing standardized care protocols and supporting research in this field can improve treatment outcomes and enhance patients’ quality of life.

**Keywords:** Targeted Therapy, Cancer, Nursing, Adverse Effects, Management

## ■ Related Factors to Spiritual Needs Among Cancer Patients: A Systematic Review

Nasrin Dadashi<sup>1</sup>, Lella Khanali Mojen<sup>2,\*</sup>

<sup>1</sup>Student Research Committee, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: leilakhanali@gmail.com

### Abstract

**Background:** Spiritual needs are important elements of holistic care, and these needs increase drastically after a diagnosis of cancer. Many cancer patients contemplate the meaning and purpose of life and issues surrounding death. Awareness of factors related to spiritual needs is an important step in comprehensive oncology care. Therefore, this systematic review investigated the factors related to spiritual needs among cancer patients.

**Methods:** A systematic review was conducted using three scientific databases: PubMed, Scopus, and Web of Science. Keywords such as “spirit”, “spiritual need”, “spiritual demand”, “cancer”, “tumour”, “oncology”, “malignancy”, “benign”, “tumor”, “neoplas” and “carcinoma” were used up to May 8, 2024. Only observational studies were included, and their qualitative assessment was conducted using the Newcastle-Ottawa Scale for cohort and cross-sectional studies.

**Results:** Out of 3613 research papers found, 13 were included in the study. The perspectives of 2855 cancer patients were investigated, of whom 970 were men and 1885 were women. Factors affecting spiritual needs were categorized into six categories: Physical (pain intensity, physical function, cancer-related fatigue), psychological (anxiety, depression, stress, demoralization), social (religious affiliation, reading the Holy Quran, social support), demographic (age, gender, race, education level, occupation, household income, number of children, marital status), clinical (duration of being diagnosed with cancer, type of treatment, disease stage, hospitalization frequency), and overall health (quality of life, satisfaction) factors.

**Conclusions:** Spiritual needs assessment is an important step in palliative and supportive care and should be considered in the planning of spiritual care based on the patient’s preferences. Identifying related factors helps healthcare providers offer comprehensive and targeted spiritual care according to the characteristics of cancer patients. Promotion of spiritual interventions helps fulfill spiritual needs and improve spiritual well-being and quality of life for cancer patients, which is the ultimate goal in palliative care.

**Keywords:** Spiritual Needs, Cancer Patients, Spirituality, Palliative Care

## ■ Pandemic Lessons for Palliative Care: A Thematic Analysis of Medical Notes Related to COVID-19

Azam Eshaghian Dorcheh<sup>1,3,\*</sup>, Ramin Kaviani<sup>2,3</sup>, Zahra Sadri<sup>3</sup>, Sara Dehghani<sup>3</sup>, Nafiseh Heidarzadeh Isfahani<sup>3</sup>, Homayoon Naji Esfahani<sup>3,4</sup>, Mohammad Sajad Zare<sup>3</sup>

<sup>1</sup>Kashani Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>2</sup>Seyed-al-Shohada Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>3</sup>Iranian Cancer Control Center (MACSA), Isfahan, Iran

<sup>4</sup>Faculty of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran

\* Corresponding Author: Azam.eshaghian@yahoo.com

## Abstract

**Background:** Although the COVID-19 pandemic wreaked havoc on palliative care (PC), the ability to overcome future crises owes to the lessons learned from this catastrophe. Home-based palliative care (HBPC) is the main setting for PC delivery in countries with non-integrated PC. While nearly half of the world population live and die in such countries, little is known about their experience with HBPC during the pandemic. This qualitative study aims to fill this gap by exploring the COVID-19 pandemic as experienced by the chief provider of HBPC in Iran, a country with isolated PC provision.

**Methods:** We performed a thematic analysis of the medical notes with a valid mention of COVID-19-related terms extracted from the medical records of biopsy-confirmed advanced cancer patients (PPS < 60) enrolled in the Iranian Cancer Control Center (MACSA) homecare program (N = 2800). The notes were generated during homecare visits or telephone consultations conducted between February 19, 2020, and May 5, 2023, during the COVID-19 pandemic in Iran.

**Results:** In total, 1,250 home care visits and telephone counseling reports from 617 patients were labeled with 1,476 codes. The findings emerged in three themes: Challenges caused by the pandemic for home-hospitalized cancer patients, barriers that impeded the provision of HBPC during the pandemic, and adaptations that could enhance HBPC during the COVID-19 health crisis.

**Conclusions:** This study summarizes the pandemic encounter experience of the palliative homecare network in Iran as representative of countries with isolated PC provision. Our findings shed light on the challenges that communities where isolated providers play a key role in PC may face during a pandemic-scale health crisis and suggest corresponding solutions.

**Keywords:** Quality of Life, COVID-19, Thematic Analysis, Palliative Home Care

## ■ Evidence-Based Symptom Management: The Role of Oncology Nurses in Improving Patient Outcomes

Maryam Jafari <sup>1,\*</sup>

<sup>1</sup>Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran. Email: maryamjafari.mj.99@gmail.com

## Abstract

**Background:** Oncology nursing is at the forefront of cancer care, addressing not only disease management but also the holistic needs of patients. Symptom manage-

ment remains a critical aspect of nursing interventions, as patients undergoing cancer treatment often experience a range of distressing symptoms, including pain, fatigue, and nausea. Evidence-based approaches to symptom management can significantly enhance patient outcomes, improving quality of life and treatment adherence. This study aims to synthesize current evidence on oncology nursing interventions in symptom management, evaluate their effectiveness, and identify best practices for implementation in clinical settings.

**Methods:** A systematic review of peer-reviewed articles up to 2023 was conducted using databases such as PubMed, Cochrane Library, and Google Scholar. Keywords included "oncology nursing", "symptom management", "evidence-based practice", and "patient outcomes". Studies were selected based on relevance and focus on nursing-led interventions. Data were extracted and analyzed based on PRISMA guidelines.

**Results:** Key findings included: 1- Pain management: Integrative approaches combining pharmacological and non-pharmacological strategies were most effective.

2- Fatigue reduction: Exercise programs and cognitive-behavioral therapy significantly reduced cancer-related fatigue.

3- Nausea control: Nurse-led education on antiemetic use improved symptom control and reduced hospital readmissions.

4- Psycho-social support: Mindfulness-based interventions and counseling enhanced emotional resilience and reduced anxiety.

**Conclusions:** The integration of evidence-based symptom management methods into oncology nursing practice is essential for enhancing patient outcomes. Future efforts should focus on training programs, interdisciplinary collaboration, and the development of accessible resources for oncology nurses.

**Keywords:** Oncology Nursing, Symptom Management, Evidence-Based Practice, Patient Outcomes, Cancer Care

## ■ The Effectiveness of Nursing Care on Sexual Function After Bladder Cancer Surgery

Fateme Rezaeeniya <sup>1,\*</sup>, Fateme Hasandoost <sup>2</sup>, Amir Reza Abedi <sup>3</sup>, Alireza Amanollahi <sup>4</sup>, Soolmaz Moosavi <sup>3</sup>

<sup>1</sup>Student Research Committee, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Men's Health and Reproductive Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>4</sup>Trauma and Injury Research Center, Iran University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Student Research Committee, Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: Fatemerezaeeniyau@gmail.com

## Abstract

**Background:** Bladder cancer surgery can lead to signifi-

cant post-operative sexual dysfunction, a distressing issue often overlooked in patient care. While various treatments exist, they often do not fully address the needs of patients recovering from major cancer surgery. Nursing care is crucial in supporting patients through their cancer journey; however, there is limited evidence regarding the effectiveness of structured, nursing-led interventions specifically targeting post-surgical sexual dysfunction after bladder cancer resection. This study aims to contribute to the evidence base by examining how a focused nursing intervention impacts sexual health outcomes.

**Methods:** This randomized controlled trial enrolled 54 bladder cancer patients in Tehran, Iran (April-September 2024). Participants were randomly assigned to either a nursing-led intervention group (n = 26) or a control group (n = 28). Sexual function was assessed using the Larson Sexual Satisfaction Questionnaire, International Index of Erectile Function (IIEF), and Female Sexual Function Index (FSFI) at baseline and at one and three months post-intervention.

**Results:** The nursing-led intervention group demonstrated a statistically significant improvement in overall sexual satisfaction ( $P < 0.001$ ) compared to the control group. Further analysis revealed significant improvements specifically in male sexual function, with statistically significant enhancements in orgasm ( $P = 0.049$ ) and sexual desire ( $P = 0.020$ ). Although the intervention did not result in significant overall changes in female sexual function scores, the analysis showed that a higher number of past medical conditions ( $P = 0.019$ ) and having a partner employed as a housekeeper ( $P = 0.017$ ) were significantly associated with lower sexual function scores among female participants.

**Conclusions:** This structured, nursing-led intervention demonstrates significant positive effects on sexual function, particularly in men, in bladder cancer patients post-tumor resection surgery. The findings highlight the potential for nursing-led interventions to play a key role in addressing the often-overlooked issue of post-surgical sexual dysfunction. However, the study also reveals that the same intervention may not be equally effective for all patients, and further research is needed to develop tailored nursing interventions that address the specific needs of female patients experiencing sexual dysfunction after surgery. This research is critical to ensure that all patients have the best opportunity to regain sexual health after bladder cancer treatment.

**Keywords:** Bladder Neoplasms, Nursing Care, Sexual Dysfunction, Postoperative Care

## ■ Death Literacy: A Narrative Review Study

Naiire Salmani <sup>1,\*</sup>, Imane Bagheri <sup>2</sup>

<sup>1</sup>Meybod Nursing School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

<sup>2</sup>Nursing and Midwifery School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

\* Corresponding Author: Meybod Nursing School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: n.salmani@ssu.ac.ir

### Abstract

**Background:** Life and death are intertwined phenomena that form a whole. Accordingly, awareness of death, acceptance of death, adaptation to death, understanding grief, the ability to mourn, and returning to normal functioning after grief are situations that require awareness raising for families. This study aimed to describe death literacy.

**Methods:** This narrative review was conducted by searching for articles using keywords such as “death literacy”, “death” and “dying” through Google Scholar, PubMed, and Scopus databases from 2016 to 2024. A total of 15 articles were retrieved and analyzed.

**Results:** Death literacy refers to “knowledge and skills that enable individuals to understand and make informed choices about end-of-life and death care options”. Individuals and communities with high levels of death literacy possess specific background knowledge about the death system and the ability to apply that knowledge. Such skills strengthen the capacity of individuals and communities to care for each other in the final stages of life, death, loss, and grief, and help individuals plan and prepare family, friends, and colleagues for changes over time and future needs. The development of death literacy in the family helps clarify many issues, including the phenomenon of death, the impact of the death of loved ones on individuals and family members, grief reactions, and how to talk about death with children. Thus, death education is crucial in developing death and grief literacy. However, death education should be provided by considering the developmental and sociocultural characteristics of families. Issues such as playing the role of caregiver before the death of parents, the experience of the death of parents, end-of-life care experience, and working with dying people, both personally and professionally, are among the factors affecting death literacy.

**Conclusions:** Given that death literacy can be effective in accepting death and adapting to grief after loss, there is a need for effective planning to strengthen context-based public education focused on increasing death literacy among community members

**Keywords:** Death Literacy, End of Life, Bereavement

## ■ Challenges in Treatment and Care for Gynecological Cancers in Socially Vulnerable Women: A Narrative Review

Zakiye Ghelbash <sup>1,\*</sup>, Saedah Zeynalzad <sup>2</sup>

<sup>1</sup>Department of Mental Health Nursing, Faculty of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>2</sup>Department of Mental Health Nursing, Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Department of Mental Health Nursing, Faculty of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran. Email: z.ghelbashp@yahoo.com

## Abstract

**Background:** Women engaged in substance abuse, those experiencing homelessness, sex workers, and women living in marginalized areas are more vulnerable to health-related threats. Gynecological cancers, such as cervical and vaginal cancers, are among the threats exacerbated by the unfavorable living conditions and prevalence of high-risk health behaviors within this group. This narrative review aims to identify the therapeutic and care challenges associated with gynecological cancers among socially vulnerable women.

**Methods:** This study is a narrative review. Articles were retrieved from databases including Scopus, Science Direct, and PubMed. The selected keywords included “genital cancer”, “cervix”, “vagina”, “women”, “vulnerable”, “care” and “treatment”. Articles published in the last decade (2014 - 2024) were considered. Additionally, limiters such as OR, AND, and NOT facilitated quicker access to relevant literature.

**Results:** The findings revealed several significant challenges, including neglect of initial clinical symptoms during screening and diagnosis, lack of adherence to treatment processes, treatment discontinuation due to economic constraints and lack of insurance, weak social support, and insufficient attention to the role of high-risk behaviors such as substance use and risky sexual practices in the treatment and recovery process.

**Discussion and Conclusions:** The results indicate that socially vulnerable women diagnosed with gynecological cancers face numerous challenges during the diagnostic and therapeutic processes, influenced by various factors. These challenges can reduce their access to timely interventions and negatively impact their quality of life. Therefore, health system professionals and policymakers must develop effective and practical measures to mitigate or eliminate these barriers.

**Keywords:** Gynecological Cancers, Vulnerable Women, Care Challenges, Therapeutic Challenges, Cervical Cancer, Vaginal Cancer

## ■ The Consequences of Resilience in Family Caregivers of Patient with Cancer: A Systematic Review

Fereshteh Mollaei <sup>1,\*</sup>, Fatemeh Amrolahi Mishavan <sup>2</sup>

<sup>1</sup>Behshahr Faculty of Nursing, Mazandaran University of Medical Sciences, Behshahr, Iran

<sup>2</sup>Department of Nursing, Langroud School of Nursing and Midwifery, Guilan University of Medical Sciences, Guilan, Iran

\* *Corresponding Author:* Behshahr Faculty of Nursing, Mazandaran University of Medical Sciences, Behshahr, Iran. Email: fmknursing71@gmail.com

## Abstract

**Background:** Resilience is a dynamic process that leads to positive adaptation in crises. Since caring for a family member with cancer comes with numerous challenges,

the resilience of family caregivers can result in positive outcomes. Therefore, this systematic review aimed to investigate the consequences of resilience in family caregivers of patients with cancer.

**Methods:** A systematic search of online electronic databases, including Scopus, PubMed, Web of Science, and the Scientific Information Database (SID), was performed using keywords extracted from medical subject headings such as “Psychological Resilience”, “Caregiver” and “Cancer” from 2014 to November 21, 2024. The quality of the studies included in this review was evaluated using the appraisal tool for cross-sectional studies (AXIS tool).

**Results:** Out of a total of 2,157 studies, 21 articles were ultimately included in the study. Most studies indicated that family caregivers possess high levels of resilience. The results related to the resilience of family caregivers include psychological benefits (reduced incidence of depression and anxiety, decreased emotional and psychological distress, greater cognitive restructuring, reduction of post-traumatic stress symptoms and improvement, post-traumatic growth, psychological well-being, benefit finding, personal growth, adaptation to new circumstances), social benefits (improved perceived social support, enhanced quality of life, greater preparedness for decision-making as substitutes, strengthened and deepened relationships with patients and relatives, reinforced sense of togetherness, feeling like a normal member of society, altruistic behaviors, role adjustment, increased capacity for empathy), reduced caregiving burden (in physical, financial, and psychological dimensions), and a greater sense of closeness to or enhanced trust in God.

**Conclusions:** Considering the positive results of resilience in family caregivers, healthcare managers and policymakers can significantly assist these individuals by developing policies and educational programs aimed at assessing, enhancing, and fostering resilience among family caregivers of cancer patients, who play a crucial role in the healthcare system.

**Keywords:** Cancer, Caregiver, Psychological Resilience, Systematic Review

## ■ Nursing Role in Management of Chemotherapy Extravasation

Marjan Dallminofar <sup>1,\*</sup>

<sup>1</sup>Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: Minoofarr1995@gmail.com

## Abstract

**Background:** Chemotherapy extravasation is a serious complication that occurs when chemotherapy drugs accidentally leak from a vein into surrounding tissues. This can lead to tissue damage, severe pain, infection, and in severe cases, tissue necrosis. Given the increasing use of chemotherapy in the treatment of various cancers, the

importance of preventing and managing this complication has become increasingly apparent. The aim of this review study was to provide an overview of chemotherapy extravasation, its risk factors, prevention methods, and management strategies.

**Methods:** A comprehensive approach was used to search for relevant articles in reputable databases such as PubMed, CINAHL, and Cochrane. Strict inclusion and exclusion criteria were applied to select studies.

**Results:** The findings of this study showed that various factors, including the type of drug, drug dose, infusion duration, needle size, injection site, and nurse skill, contribute to the occurrence of chemotherapy extravasation. Prevention methods include selecting an appropriate injection site, using suitable needles, securing the needle, continuous monitoring of the injection site, and educating healthcare personnel. If extravasation occurs, prompt and appropriate management can prevent the progression of tissue damage and subsequent complications. Treatment methods include the use of antidotes, cold or hot compresses, surgery, and drug therapy.

**Conclusions:** Chemotherapy extravasation is a serious complication that can have severe consequences for the patient. Given the importance of this issue, educating healthcare personnel, using standard protocols, and prompt and appropriate management in case of extravasation are essential measures for preventing and managing this complication.

**Keywords:** Chemotherapy Extravasation, Side Effects, Prevention, Management, Cancer

### ■ Determining Predictors of Subjective Financial Distress in Cancer Patients

Alireza Javanmardi <sup>1</sup>, Alireza Momeni <sup>2</sup>, Hadis Ashrafzadeh <sup>3,\*</sup>, Mobina Nabizadeh <sup>4</sup>

<sup>1</sup>Student Research Committee, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

<sup>2</sup>Department of Internal Medicine, School of Medicine, Ganjavian Hospital, Dezful University of Medical Sciences, Dezful, Iran

<sup>3</sup>School of Nursing, Dezful University of Medical Sciences, Dezful, Iran

<sup>4</sup>Student Research Committee, Dezful University of Medical Science, Dezful, Iran

\* *Corresponding Author:* School of Nursing, Dezful University of Medical Sciences, Dezful, Iran. Email: Ashrafzadeh.h1993@gmail.com

#### Abstract

**Background:** Cancer is very costly and has multiple adverse effects on various individual, family, social, and economic dimensions, which not only disrupt the individual's life but also adversely affect all family members. Since the concept of mental financial distress is a new issue in Iran, it is important to examine its relationship with the aforementioned variables. Therefore, this study aimed to determine the relationship between subjective financial distress and perceived social support, treatment adherence, and life satisfaction in cancer patients.

**Methods:** This cross-sectional descriptive-analytical study was conducted on 300 cancer patients referred to

cancer referral centers, who were randomly selected. In this study, subjective financial distress, life satisfaction, treatment adherence, and perceived social support questionnaires were used. The validity and reliability of these tools have been confirmed in cancer patients in Iranian society. The data collected were analyzed using SPSS version 24 software, employing descriptive and inferential statistics tests.

**Results:** The mean age of the participants was  $47.33 \pm 12.24$  years, with an age range of 18 - 77 years. The mean subjective financial distress score was  $21.48 \pm 4.47$ , with a range of 2 - 28. More than half of the cancer patients suffered from severe/grade 4 mental financial distress. About 63% of the cancer patients had moderate treatment adherence. The mean life satisfaction score indicated that cancer patients have moderate life satisfaction, while the mean perceived social support score showed that cancer patients receive good social support from their environment. There was no statistically significant relationship between subjective financial distress and the variables of treatment adherence ( $P = 0.06$ ,  $r = -0.108$ ) and perceived social support ( $P = 0.051$ ,  $r = -0.115$ ), but there was a statistically significant relationship between subjective financial distress and life satisfaction ( $P = 0.000$ ,  $r = -0.271$ ).

**Conclusions:** According to the findings, more than half of cancer patients have severe/grade 4 subjective financial distress, with life satisfaction being the most important predictor. Subjective financial distress negatively affects cancer patients and their families and is common among cancer patients worldwide. Consequently, in clinical practice, financial toxicity in cancer patients requires more attention. Assessment, acknowledgment, and discussion of financial toxicity are crucial milestones.

**Keywords:** Palliative Care, Financial Toxicity, Mental Financial Distress, Treatment Adherence, Life Satisfaction, Perceived Social Support

### ■ The Role of Nursing in Multifaceted Cancer Management: A Comprehensive Review of Challenges and Opportunities

Soolmaz Moosavi <sup>1,\*</sup>

<sup>1</sup>Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: Moosavi.soolmaz@yahoo.com

#### Abstract

**Background:** Oncology nurses play a vital role in the multifaceted management of cancer and, as key members of the treatment team, contribute to improving the quality of life of patients, reducing treatment complications, and promoting supportive care. Given the complexities of cancer treatment and the increasing prevalence of this disease, the need to develop comprehensive

approaches in nursing has become more important than ever. The role of nurses in the management of patients with cancer includes preventive, therapeutic, and supportive care. In the early stages of cancer diagnosis, nurses play an important role in reducing anxiety and preparing patients for the treatment path by providing appropriate education to patients and their families. During treatment, they help manage the side effects of chemotherapy, radiotherapy, and other systemic treatments. They also provide effective emotional and psychological support using communication skills, which significantly impacts the acceptance of treatment and the quality of life of patients. This article aims to comprehensively review the role of nursing in oncology, analyze challenges, and provide solutions to improve the quality of nursing care.

**Methods:** This review was conducted by reviewing reputable scientific articles and texts published in databases such as PubMed, Scopus, and Google Scholar. The selected studies included articles that addressed the role of nursing, challenges, and opportunities in caring for cancer patients.

**Results:** The findings of this review show that nurses play a prominent role in various areas, including managing side effects of treatment, providing psychosocial support, and educating patients. However, challenges such as job stress, shortage of human resources, and the need for specialized training are among the main problems in this field. The use of new technologies such as telemedicine and artificial intelligence has provided opportunities to improve the efficiency and quality of nursing services.

**Conclusions:** Despite numerous challenges, the development of advanced training, increased interprofessional collaboration, and the use of new technologies can improve the quality of care. Strengthening organizational support and providing solutions to reduce job stress can help maintain and enhance this role. Additionally, research in the field of cancer nursing, providing evidence-based interventions, and increasing interprofessional collaboration can enhance the role of nurses in health care systems

**Keywords:** Oncology, Nursing, Care, Cancer

### ■ Related Factors to Death Anxiety Among Cancer Patients: Cross-Sectional Study

Somayeh Bahrami <sup>1,\*</sup>, Fatemeh Kamali <sup>2</sup>

<sup>1</sup>Department of Nursing, Faculty of Nursing and Midwifery, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran

<sup>2</sup>Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Nursing, Faculty of Nursing and Midwifery, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran. Email: Somayeh.bahrami@iautmu.ac.ir

#### Abstract

**Background:** Death is an inevitable reality for all humans, yet it can be a source of anxiety due to its ambiguous nature. In particular, death anxiety increases in patients with life-threatening and refractory diseases, such as cancer. Death anxiety, as a negative consequence of cancer, influences the lives of many patients after detection and treatment. Various demographic, clinical, and psychological factors can impact patients' experiences of death anxiety. This study aimed to determine the factors related to death anxiety among cancer patients.

**Methods:** This descriptive and cross-sectional study was conducted on cancer patients in the oncology wards and clinics of a hospital in Tehran, Iran. Two hundred eligible patients, selected by purposeful sampling, completed a clinical and demographic questionnaire and Templer's Death Anxiety Scale (DAS). The data were analyzed using SPSS version 20 software.

**Results:** The participants' mean age was  $54.01 \pm 8.25$  years, and the average illness period was  $7.22 \pm 4.10$  months. Males and females constituted 57% and 43% of the patients, respectively, with 82% being married. Gastrointestinal cancers were prevalent among the patients (74%), and 87% had undergone chemotherapy in the last month. The participants' mean DAS score was  $6.99 \pm 1.94$ . Age, gender, marital status, occupational and economic circumstances, and type of cancer were statistically significant predictors of death anxiety ( $P < 0.05$ ).

**Conclusions:** Due to their life-threatening nature, chronic diseases such as cancer can be the source of numerous psychological challenges, including death anxiety. The researchers recommend mental assessment in oncological care to identify psychological challenges and achieve the ultimate goal of palliative care, which is improving patients' quality of life.

**Keywords:** Death Anxiety, Cancer Patients, Palliative Care

### ■ Silent Suffering: Hidden Psychological Effects on Husbands of Women with Breast Cancer

Nasrin Shabani <sup>1,\*</sup>, Mohammad Aghajani <sup>2</sup>, Negin Masoudi Alavi <sup>1</sup>

<sup>1</sup>Nursing Trauma Research Center, Kashan University of Medical Sciences, Kashan, Iran

<sup>2</sup>Infectious Diseases Research Center, Department of Psychiatric Nursing, Kashan University of Medical Sciences, Kashan, Iran

\* *Corresponding Author:* Nursing Trauma Research Center, Kashan University of Medical Sciences, Kashan, Iran. Email: Nasrinshabani5@gmail.com

#### Abstract

**Background:** A diagnosis of breast cancer in women not only affects the patients but also imposes significant psychological challenges on their husbands. This study aimed to investigate the prevalence and severity of depression, anxiety, and stress among husbands of women with breast cancer and highlights the often overlooked emotional complications in these caregivers.

**Methods:** A cross-sectional study was conducted on 265 husbands of women with breast cancer from health cen-

ters in Kashan, Iran in the first half of 2013. Psychological distress was assessed using the Depression, Anxiety, and Stress Scale (DASS-21). Data were analyzed using descriptive and inferential statistics, including regression analysis, to identify correlations between psychological outcomes and various demographic and caregiving factors.

**Findings:** About 30% of husbands exhibited significant emotional distress in the form of depression, anxiety, and stress. The severity of psychological distress was significantly associated with factors such as the wife's stage of illness, duration of caregiving, and the husband's prior mental health history.

**Discussion:** The psychological impact of breast cancer extends beyond the patients themselves and significantly affects their husbands. This study highlights the alarming prevalence of depression, anxiety, and stress among husbands of women with breast cancer and shows that these caregivers often experience profound emotional distress. These statistics underscore the urgent need for increased awareness and targeted psychological support for this often-overlooked demographic.

**Conclusions:** This study highlights an important gap in understanding the psychological challenges faced by husbands of women with breast cancer. The high prevalence of depression, anxiety, and stress among these caregivers necessitates urgent action to provide appropriate psychological support and interventions. By recognizing the unique emotional burden that husbands carry, healthcare professionals can better support their patients and their husbands, ultimately enhancing the quality of life for both parties.

**Keywords:** Breast Cancer, Husbands, Psychological Effects

### ■ Investigating the Assistance of Animals in the Palliative Care of Cancer Patients

Atousa Afsari <sup>1,\*</sup>, Mina Afsha <sup>1</sup>, Haniyeh Mohammad Poor Babae <sup>2</sup>

<sup>1</sup>Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran

<sup>2</sup>Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Iran

\* *Corresponding Author:* Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Iran. Email: Afsariatousa1@gmail.com

#### Abstract

**Background:** Palliative care is an approach to improve the quality of life of patients and their families dealing with multiple physical and mental problems related to life-threatening and chronic diseases, including cancer. Treatment with the help of animals, as a novel non-pharmacological treatment and supplement, can enhance patients' quality of life, improve communication, and increase life expectancy during the treatment process. This review study examines the role of animal assistance in the palliative care of cancer patients.

**Methods:** This systematic review was conducted using

relevant books and materials in scientific journals published in this field, and by searching for articles using the SCOPUS, IRANDOC, MAGIRAN, PubMed, and Google Scholar search engines from 2017 to the present.

**Findings:** Based on the studies conducted, the use of animals in the treatment process of cancer patients leads to improved care delivery, soothing effects, and positive psychological and physiological changes. These include improving self-esteem, reducing irritability, depression, and anger, and enhancing compatibility with the hospital environment. Visual communication and touch with animals lead to the release of various hormones, including serotonin, endorphin, and oxytocin.

**Conclusions:** Considering the effective role of animals in enhancing the efficiency of palliative care, increasing the quality of life of patients, and improving mood among cancer patients, it is expected that more specialized training will be provided for treatment staff, including doctors and nurses. Emphasizing the importance of animal assistance in palliative care, as well as implementing necessary measures and precautions to ensure the physical and psychological well-being of patients, should be integrated into the care and treatment process.

**Keywords:** Palliative Care, Cancer, Animals

### ■ Palliative Care Model Integrated with PHC and Quality of Life Caregivers of Ill Cancer Patients

Heshmatolah Heydari <sup>1,\*</sup>, Hadisossadat Hosseini <sup>2</sup>, Maryam Rassouli <sup>3</sup>

<sup>1</sup>School of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran

<sup>2</sup>Student Research Committee, School of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran

<sup>3</sup>Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* School of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran. Email: Hidari.h@lums.ac.ir

#### Abstract

**Background:** Cancer diagnoses are on the rise, inflicting devastating pain and suffering on patients, especially in the final months of life. To relieve these patients, palliative care can be provided in various models. The effectiveness of community-based palliative care provided through a primary health care (PHC) approach in cancer patients has not been studied. Therefore, this study aimed to determine the impact of the integrated palliative care model with PHC on the quality of life of caregivers of ill cancer patients.

**Methods:** This was a randomized controlled trial. The research population included 120 cancer patients and their family caregivers referred to comprehensive health centers in Khorramabad in the second half of 2023. Sampling was carried out using the convenience sampling method, and then the subjects were divided into two groups — intervention and control — through random blocks of size four. Subjects in the intervention group received PHC-

integrated community-based palliative support for two months, while their control counterparts received their typical health care programs over the same period. The Quality of Life in Life-Threatening Illness-Family Caregiver Questionnaire was used before and two months after the intervention for gathering information. The data were analyzed using SPSS version 22 software and descriptive and inferential statistics.

**Results:** Data analysis showed no significant difference between the two study groups in terms of demographic characteristics. After the intervention, a paired t-test showed a statistically significant difference in the mean scores of all dimensions of family caregivers' quality of life, except for the physical and financial dimensions, in both groups ( $P < 0.05$ ). Regarding the overall quality of life score, caregivers in the intervention group scored significantly higher ( $101.39 \pm 12.50$ ) compared to the control group ( $90.06 \pm 5.33$ ,  $P < 0.01$ ).

**Conclusions:** Integrated palliative care with PHC can promote the quality of life of caregivers of patients with cancer. Therefore, it is suggested that policymakers consider community-based palliative care to improve the quality of life of the families of these patients.

**Keywords:** Quality of Life, Advanced Cancer Patients, Palliative Care, Primary Health Care, Caregiver

### ■ Examining Cultural-Related Ethical Challenges in the Care of Cancer Patients

Mina Afshar<sup>1,\*</sup>, Atousa Afsari<sup>1</sup>, Haniyeh Mohammad Poor Babae<sup>1</sup>

<sup>1</sup>Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran

\* Corresponding Author: Department of Nursing, School of Nursing and Midwifery, Takestan Branch, Islamic Azad University, Takestan, Iran. Email: M.afshar0913@gmail.com

#### Abstract

**Background:** Cancer, as one of the complex and significant diseases of contemporary times, poses not only clinical and therapeutic challenges but also extensive ethical issues. In the process of caring for cancer patients, decisions such as disclosing diagnoses, selecting appropriate treatments, and end-of-life care hold particular importance. These decisions, in addition to universal ethical principles such as autonomy, beneficence, non-maleficence, and justice, are profoundly influenced by cultural and social contexts. Culture can significantly affect how patients perceive their illness and treatment, as well as their expectations from healthcare providers. For example, in some cultures, full disclosure of a cancer diagnosis may face resistance, while in others, patients may expect to be fully informed about their condition. This cultural diversity can create multiple ethical challenges in the decision-making process. This review article aims to analyze these challenges and provide strategies for managing them. By examining the existing literature

and analyzing various cases, the goal is to achieve a better understanding of how culture impacts ethical challenges in the care of cancer patients and to offer recommendations for improving the quality of care and ethical decision-making in this field.

**Method:** This study was designed as a systematic review, examining articles published between 2010 and 2023 from reputable international databases including PubMed, Scopus, Web of Science, Google Scholar, as well as Persian sources such as SID, Magiran, and IranMedex. The criteria for selecting articles included direct relevance to the topic, high quality, and publication in reputable journals.

**Results:** One of the main challenges in the care of cancer patients is the conflict between patient autonomy and families' requests for concealment. In collectivist cultures, such as Iran, families often believe that concealing the diagnosis from the patient can help maintain their morale. However, in individualistic cultures, transparency and informing the patient are considered an ethical duty. Studies have shown that physicians in collectivist societies sometimes resort to concealment to preserve social and familial relationships. In end-of-life care, religious and cultural values play a significant role in decision-making. In religious cultures, life is viewed as a divine gift, and the cessation of aggressive treatments is sometimes seen as neglecting the value of life. In contrast, in individualistic societies, the focus is prioritized on quality of life, and palliative care is preferred as an ethical option. Justice in the allocation of treatment resources for cancer patients is another fundamental challenge. In developing societies, limited financial and medical resources often lead to inequalities in patients' access to treatment. These disparities can arise from social, economic, and cultural factors, impacting ethical decision-making.

**Conclusions:** The ethical challenges in the care of cancer patients are significantly influenced by cultural and social factors. Managing these challenges requires the formulation of guidelines that integrate universal ethical principles with cultural values. Educating healthcare teams to enhance awareness of cultural and ethical sensitivities is essential. Transparent and participatory dialogues among physicians, patients, and families can help build trust and reduce conflicts. Additionally, the development of palliative care services plays a crucial role in alleviating the physical and psychological burdens on patients and their families.

**Keywords:** Ethical Challenges, Cultural Factors, Cancer Care, Patient Autonomy, End-of-Life Care

### ■ The Role of Nurses in Communicating Bad News to Patients and Families: An Integrated Review Study

Soore khaki<sup>1,\*</sup>, Masoud Fallahi Khoshknab<sup>2</sup>, Farahnaz Mohammadi Shabboulagh<sup>2</sup>, MohammadAli Hosseini<sup>2</sup>

<sup>1</sup>Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Nursing, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

\* *Corresponding Author:* Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: skhaki170@gmail.com

## Abstract

**Background:** Given that nurses serve as a vital link between physicians, patients, and their families, focusing on their role in conveying difficult news is essential. This review seeks to outline and emphasize the significance of nurses in delivering bad news to patients and their families.

**Methods:** This was an integrated review. To collect data, a literature search was conducted in the Persian and English databases of Magiran, Scientific Information Base (SID), Scopus, Google Scholar, Web of Science, and PubMed. Eligibility criteria included publications in English and Persian between January 1, 1980, and January 1, 2022, describing the role of nurses in delivering bad news to patients and families. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were used to screen and select relevant studies. Critical appraisal tools provided by the Joanna Briggs Institute (JBI) were used for quality assessment. The collected data were analyzed using constant comparative methods.

**Results:** Of the 453 unique records screened, only 26 met the eligibility criteria. The results show that delivering bad news is a team process in which nurses have several roles. Their main roles were classified into four categories: Manager, facilitator, educator, and supporter/advocate, with 74 subordinate roles.

**Conclusions:** The role of nurses in conveying adverse news to patients and their families is crucial. Their communication skills and interpersonal behaviors profoundly influence how this information is perceived. Failure to acknowledge the nurses' role in this process may undermine the patient's trust and comprehension of the quality of care provided. Consequently, nurses must receive specialized training in delivering bad news and offering support to patients and families during challenging circumstances.

**Keywords:** Role of Nurses, Delivering Bad News, Truth Disclosures, Integrated Review

## ■ Telemedicine: Missing Link in Breast Cancer Palliative Care

Shima Yadegar Tirandaz <sup>1,\*</sup>

<sup>1</sup>Student Research Committee, Department of Community Health Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Student Research Committee, Department of Community Health Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: shima.yadegar@yahoo.com

## Abstract

**Background:** Breast cancer, the most common cancer in women, is associated with high morbidity and mortality. Palliative care, recognized as a human right in health, faces challenges in access within the healthcare systems of low-income countries. Telemedicine presents an opportunity to address this challenge. This study was conducted to review the importance and role of telemedicine in palliative care.

**Methods:** This review involved an examination of original articles in the databases PubMed, Scopus, Web of Science (WOS), and Google Scholar using the keywords "Breast cancer", "Telemedicine" and "Palliative care" up to December 2024. A total of 13 studies related to the aim were included.

**Results:** Telemedicine aims to overcome geographical distances and ease access to health professionals and caregivers while reducing the costs of frequent visits. It helps maintain a good therapeutic relationship and continuity of care. Additionally, it facilitates multidisciplinary cooperation among the care team and provides comprehensive and integrated care, helping to better identify and meet the needs of breast cancer patients and their families, quickly respond to changes, and increase patient satisfaction and quality of life. With the positive effects of social support, telemedicine plays an effective role in promoting self-care and increasing patient survival.

**Conclusions:** Telemedicine is a valuable tool in providing patient-centered, high-quality, and timely palliative care by expanding access to palliative care and reducing the burden on employees and the healthcare system. It is essential for supporting and caring for patients with breast cancer and their families.

**Keywords:** Breast Cancer, Telemedicine, Palliative Care

## ■ Outcomes of Oncology Nurse Navigator in Palliative Care: A Review Study

Shima Yadegar Tirandaz <sup>1,\*</sup>

<sup>1</sup>Student Research Committee, Department of Community Health Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* *Corresponding Author:* Student Research Committee, Department of Community Health Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: shima.yadegar@yahoo.com

## Abstract

**Background:** Cancer patients have complex and multiple needs that impact their lives and those of their families. Interdisciplinary supportive and palliative care, as a right of individuals in health and to improve the quality of life of patients and their families, faces challenges. Nurse navigators are an innovative approach that acts as a gateway, ensuring that these individuals receive appropriate treatment and care with personalized education and referral for rehabilitation and timely palliation. Therefore, this review study aimed to investigate the im-

plications of cancer nurse navigators in palliative care.

**Methods:** This review conducted a systematic analysis of original articles in the databases PubMed, Scopus, Web of Science (WOS), and Google Scholar using the keywords “Oncology”, “Nurse Navigator” and “Palliative Care” up to November 2024. A total of 7 studies related to the aim were included.

**Results:** The outcomes of cancer nurse navigators in palliative care, based on the studies reviewed, include facilitating continuity of care, developing care treatment plans, increasing survival, facilitating patient transition and movement through the difficult path of treatment and care, promoting and improving timely access to care, enhancing communication between the patient and the cancer care team, achieving desired care treatment outcomes, reducing patient anxiety, promoting informed decision-making in patients, improving health care system processes by reducing harms caused by cancer diagnosis and uncertainty, improving the standard of oncological care, satisfaction with services, psychosocial support for patients and their families, reducing the fragmentation of care, coordinating health resources and patients’ needs, increasing patients’ health literacy, reducing treatment complications, better control of disease symptoms, managing patient costs, eliminating barriers to care, and improving the quality of health care delivery.

**Conclusions:** The roles of nurse navigators are expanding globally. Given the positive implications of this innovative approach, including enhancing patient experiences, optimizing clinical outcomes through interdisciplinary palliative care, and ensuring the safe transition of cancer patients requiring palliative care throughout their disease journey, this role should be considered by policy-makers and nursing managers in oncology.

**Keywords:** Cancer, Nurse Navigator, Palliative Care, Outcome

### ■ Evaluate the Effectiveness of Mandala Coloring on Anxiety Levels in Cancer Patients Undergoing Treatment

Zahra Ghornani<sup>1,\*</sup>

<sup>1</sup>Department of Pediatric Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\* Corresponding Author: Department of Pediatric Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: Zahraghornani178@gmail.com

#### Abstract

**Background:** Anxiety is a prevalent psychological issue among cancer patients, significantly affecting their quality of life and treatment outcomes. Art therapy, particularly mandala coloring, has emerged as a potential intervention to alleviate anxiety symptoms in this population. This study aims to evaluate the effectiveness of mandala coloring on anxiety levels in cancer patients undergoing treatment.

**Methods:** A randomized controlled trial was conducted with 100 cancer patients divided into two groups: The intervention group engaged in mandala coloring sessions, while the control group received standard care without art therapy. Anxiety levels were measured using the state-trait anxiety inventory (STAI) before and after the intervention period of four weeks.

**Results:** Preliminary findings indicate that participants in the mandala coloring group experienced a significant reduction in anxiety levels compared to the control group ( $P < 0.01$ ). The effect size was moderate, suggesting a meaningful impact of mandala coloring on anxiety reduction.

**Conclusions:** Mandala coloring appears to be an effective intervention for decreasing anxiety in cancer patients. These findings support the integration of art therapy into standard oncology care to enhance psychological well-being. Further research is warranted to explore long-term effects and potential mechanisms underlying this therapeutic approach.

**Keywords:** Mandala Coloring, Anxiety, Cancer Patients, Art Therapy, Psychological Well-Being

### ■ The Comparison of the Effect of Personalized Supportive Mobile Health and In-person Home-Based Education on the Burden of Care and Coping Strategies of Family Caregivers of Older People Cancer Patients

Shahin Salarvand<sup>1,\*</sup>, Sima Varmezayir<sup>2</sup>, Afsaneh Beiranvand<sup>3</sup>, Mohammad Aghaali<sup>4</sup>

<sup>1</sup>Hepatitis Research Center, Faculty of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran

<sup>2</sup>Student Research Committee, Faculty of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran

<sup>3</sup>Department of Nursing, School of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran

<sup>4</sup>Department of Family and Community Medicine, School of Medicine, Qom University of Medical Sciences, Qom, Iran

\* Corresponding Author: Hepatitis Research Center, Faculty of Nursing and Midwifery, Lorestan University of Medical Sciences, Khorramabad, Iran. Email: shsalarvand@lums.ac.ir

#### Abstract

**Background:** Family caregivers of older individuals with cancer bear a significant care burden. They require assistance to adapt to the situation and select effective coping strategies. This study was conducted to compare the effects of personalized supportive mobile health education (mHealth) and in-person home-based education on the care burden and coping strategies of family caregivers of older cancer patients.

**Methods:** A quasi-experimental study was conducted with random allocation of participants into two groups: In-person home-based education and mobile health education, with 30 participants in each group. Questionnaires on demographic characteristics, Zarit’s Caregiver

Burden Scale, and the coping inventory for stressful situations (CISS) were utilized. Data analysis was performed using SPSS version 16.

**Results:** The study indicated that before the intervention, there was no statistically significant difference in the level of care burden and the type of coping style between the in-person home-based education and mHealth education groups. However, after the intervention and two months post-intervention, the care burden in the in-person home-based education group was significantly reduced compared to the mHealth education group. Additionally, both groups showed a tendency towards a problem-oriented coping style, with the in-person home-based education group exhibiting a significantly higher use of this style than the mHealth education group.

**Conclusions:** This study demonstrated that both in-person home-based education and mobile health education methods are effective in reducing caregiving burden and promoting a problem-oriented coping style among family caregivers of older individuals with cancer. However, in-person home-based education was significantly more effective in achieving these outcomes.

**Keywords:** Mobile Health Education, In-person Home-Based Education, Family Caregivers, Older People with Cancer, Caregiving Burden, Coping Style

### ■ Investigating into the Application of Ferrous-Based Metal-Organic Frameworks Loaded with Paclitaxel to Enhance Radiosensitivity in Breast Cancer Radiation Therapy

Daliri Sosefi Z.<sup>1,2</sup>, Ghorbani M.<sup>1</sup>, Khoshkar Foshtomi M.<sup>3,2</sup>, Naseri A. R.<sup>5,4</sup>, Jalili J. G., Farajollahi A. R.<sup>3,2,4,\*</sup>

<sup>1</sup>Nutrition Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Department of Medical Physics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>3</sup>Medical Radiation Sciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>4</sup>Department of Radio-oncology, Shahid Madani Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>5</sup>Biotechnology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>6</sup>Department of Interventional Radiology, Department of Radiology, Emam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

\* Corresponding Author: farajollahiar@gmail.com

#### Abstract

**Background:** Cancer is a significant contributor to global mortality. One of the primary reasons for treatment failure and tumor recurrence is the development of resistance to therapeutic methods. Utilizing innovative and targeted strategies, particularly through the design of purposeful nanostructures with multifunctional applications, has gained interest in chemoradiotherapy. This ap-

proach aims to enhance the radiosensitization of tumor tissues while concurrently reducing unnecessary damage to surrounding healthy organs. In the present work, ferrous-based nanoscale metal-organic frameworks (Fe-MOFs), as a class of hybrid materials consisting of Fe<sup>2+</sup> ions and organic ligands, were tested. These frameworks can trigger the Fenton reaction and promote the generation of reactive oxygen species (ROS) during tumor irradiation, leading to apoptosis and necrosis of cancer cells.

**Methods and Materials:** Bovine serum albumin (BSA) was coated on Fe-MOF@PTX to promote stability in the physiological environment. Fe-MOFs were evaluated as potential drug-releasing nanoparticles, aiming to enhance paclitaxel (PTX) solubility and promote radiation sensitivity in the MCF-7 breast cancer cell line during radiotherapy. The cellular study groups comprised a control group, a group undergoing PTX treatment, groups treated with nano Fe-MOFs, and Fe-MOF@PTX, which were examined in the presence and absence of radiation. Prepared samples were exposed to doses of 2, 4, and 8 Gy, using energies of 6 and 15 MV. Subsequently, assays including uptake, MTT, apoptosis, DAPI, and ROS were employed to determine cell survival rates, anticancer effects, and increased radiation sensitivity.

**Results:** The synthesis of Fe-MOF@PTX-BSA was confirmed by dynamic light scattering (DLS) and transmission electron microscopy (TEM). Successful drug loading was confirmed through Fourier-transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), and Brunauer-Emmett-Teller (BET) analyses, and drug release assessments. The Fe-MOF exhibited suitable hemolytic properties at various concentrations. The biosafety profile of Fe-MOFs demonstrated favorable results in MTT tests conducted on both human umbilical vein endothelial cells (HUVEC) and MCF-7 cells. Anticancer effects and enhanced radiosensitivity of the nanosystem and final nanostructure were validated using MTT (24 and 48 hours), apoptosis, ROS, and DAPI assays under both irradiated and non-irradiated conditions. Overall, cell death and apoptosis resulting from a substantial induction of ROS were observed in cancer cells treated with the nanosystem and final nanostructure in conjunction with X-ray radiation.

**Conclusions:** The in vitro experiments demonstrated that Fe-MOF@PTX-BSA, alongside X-ray radiation, activated a substantial in situ generation of ROS, consequently contributing to increased radiosensitivity in MCF-7 cells and apoptosis. Notably, no significant differences in the results were observed between 6 and 15 MV of radiation. This may underscore the synergistic effectiveness of Fe-MOF-BSA nanoparticles, affirming their role as both a drug carrier and radiosensitizer in this study.

**Keywords:** Fe-MOF Nanoparticles, Chemo-radiotherapy, Radiation Sensitizer, MCF-7, Paclitaxel

## ■ Radiotherapy in the Management of Graves' Ophthalmopathy: A Systematic Review

Sahar Seif <sup>1, \*</sup>, S. Mahdi Shams Zadeh Alavi <sup>2</sup>, Sophia Salehi <sup>2</sup>, Fatemeh Sadat Hosseini <sup>2</sup>, Kimia Rahimi <sup>2</sup>, Armita Zanjani <sup>2</sup>

<sup>1</sup>Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran

<sup>2</sup>Student Research Committee, Arak University of Medical Sciences, Arak, Iran

\* *Corresponding Author:* Department of Medical Physics and Radiotherapy, Khansari Hospital, Arak University of Medical Sciences, Arak, Iran. Email: sahar\_s59@yahoo.com

### Abstract

**Background:** Graves' ophthalmopathy (GO) is an ocular inflammatory disease that threatens vision and significantly impacts patients' quality of life. Despite various treatments such as corticosteroids, surgery, and biologics, challenges remain due to adverse effects and inconsistent efficacy. Emerging evidence supports radiotherapy (RT) as a beneficial treatment for GO, characterized by a favorable side effect profile. This systematic review investigates the effects of different radiotherapy modalities in managing this condition.

**Methods:** Following PRISMA guidelines, we conducted a comprehensive review of PubMed, Embase, Scopus, and Web of Science, along with reference lists of relevant papers, to identify studies on Graves' ophthalmopathy and radiotherapy published up to December 2024.

**Results:** Out of 664 initial articles, 70 studies were selected based on the inclusion criteria. These studies included 22 original articles, 15 case reports, 12 in vivo studies, 16 in vitro studies, and 5 reviews. The findings indicate that radiotherapy plays a significant role in the treatment of GO, especially in patients who are inoperable or resistant to other treatments.

**Conclusions:** Radiotherapy is effective in managing Graves' ophthalmopathy by reducing inflammation and improving visual acuity and symptoms such as diplopia and ocular dryness. It is particularly beneficial in advanced stages of the disease and has fewer side effects than traditional treatments. However, concerns about RT's impact on healthy tissues persist, especially with three-dimensional radiotherapy (3D-RT). Advanced techniques like intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) enhance precision and may provide significant benefits for patients with inoperable or treatment-resistant GO while minimizing adverse effects. Integrating these methods into combined treatment protocols could improve patient quality of life.

**Keywords:** Radiotherapy, Graves' Ophthalmopathy, Treatment

## ■ Enhancing the Response of Resistant Renal Cancer Tumors to Megavoltage X-rays Using Cold Atmospheric Plasma as a Radiosensitizer

Hanieh Nazem Zomorodi <sup>1, \*</sup>, Seyed Mahmoud Reza Aghamiri <sup>1</sup>, Fatemeh Pak Niyat <sup>2, 3</sup>, Aziz Mahmoud Zadeh <sup>4</sup>, Abolfazl Razzagh Doust <sup>5</sup>, Hamid Reza Ghomi <sup>6</sup>, Bahram Mofid <sup>5</sup>

<sup>1</sup>Department of Medical Radiation Engineering, Shahid Beheshti University, Tehran, Iran

<sup>2</sup>Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Radiation Biology Studies, Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>4</sup>Faculty of Passive Defense, Malek Ashtar University of Technology, Tehran, Iran

<sup>5</sup>Urology and Nephrology Research center, Research Institute for Urology and Nephrology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>6</sup>Laser and Plasma Research Institute, Shahid Beheshti University, Tehran, Iran

\* *Corresponding Author:* Department of Medical Radiation Engineering, Shahid Beheshti University, Tehran, Iran. Email: hanieh.zomorodi2966@yahoo.com

### Abstract

**Background:** Radiation therapy is rarely used for kidney cancer due to the high resistance of kidney cancer cells. Radiosensitizers, such as cold atmospheric plasma (CAP), can increase cancer cells' sensitivity to radiation, allowing for lower doses of X-ray radiation and fewer side effects. The CAP, delivered via a plasma jet, uses a mixture of 95% argon and 5% oxygen gas to produce reactive oxygen species (ROS) that can destroy cancer cells. The CAP's selective action is due to its higher ROS production in cancer cells compared to normal cells, leading to greater apoptosis in cancer cells. This study used clonogenic assays to measure the effectiveness of combined CAP and radiation treatments, showing CAP's potential as a radiosensitizer. Evaluations included apoptosis measurement, ROS production quantification, and cell cycle analysis.

**Materials and Methods:** 1. Clonogenic assay: Plating efficiency, representing the percentage of cultured cells forming colonies, was determined across different treatments (control, 2 Gy radiation, CAP, and their combination). Cell lines were cultured in 25 cm<sup>2</sup> flasks at low cell densities and treated after 24 hours. Post-treatment, cells were incubated for 10 - 14 days for colony formation. Colonies were then stained with crystal violet and counted, with survival rates calculated.

2. Apoptosis assay by annexin flow cytometry: The type and extent of cell death in HEK293 and ACHN cells across four treatment groups were determined using flow cytometry and an apoptosis kit. Cells were treated, incubated according to their doubling times, and stained with Annexin V-FITC and PI. Fluorescence levels were measured using a flow cytometer to determine apoptosis rates.

3. Cell cycle arrest by flow cytometry: Flow cytometry was utilized to examine the impact of different treatments on the cell cycle status of HEK293 and ACHN cells. Post-treatment, cells were incubated, fixed, stained with PI MASTER

MIX, and fluorescence levels were measured to analyze cell cycle phases.

4. ROS test by flow cytometry: The ROS levels in HEK293 and ACHN cells were determined across different treatments using flow cytometry. Cells were treated, incubated, stained with DA-DCFH and PI dyes, and fluorescence levels were measured to assess ROS production.

**Results:** The clonogenic assay showed that normal and tumor kidney cells had survival rates of 90.12% and 80.80% at a 2 Gy dose, confirming their radioresistance. The CAP treatment decreased survival rates to 28.71% (normal) and 4.55% (tumor), indicating high sensitivity to CAP. Combined CAP and 2 Gy irradiation further reduced survival to 13.07% (normal) and 0.49% (tumor), showing a synergistic effect. Annexin flow cytometry showed that 2 Gy radiation did not induce significant apoptosis in HEK293 or ACHN cells. The CAP treatment increased apoptosis 8.98 times in HEK293 and 19.73 times in ACHN. Combined treatment amplified apoptosis in HEK293 (10.46 times) and ACHN (20.9 times), highlighting CAP's selective action and synergy with irradiation. Cell cycle tests revealed a high frequency of the Sub-G1 phase in ACHN under CAP and combined treatments, indicating substantial apoptosis. Combined treatment increased the Sub-G1 population by 17.02 times. The ROS test also confirmed the above results.

**Conclusions:** The results of clonogenic survival, apoptosis, cell cycle, and ROS assays indicated that kidney cancer cells are highly radioresistant, often rendering conventional radiotherapy ineffective. However, these cells show high sensitivity to CAP, which induces apoptosis even with indirect irradiation. Combining CAP with 2 Gy radiation has a synergistic effect, significantly increasing cell destruction. Apoptosis tests showed 16.92 times more cell death with the combined treatment compared to 2 Gy radiation alone, while cell cycle tests showed a 31.32 times increase in apoptotic cells. This suggests that CAP, as a radiosensitizer, could be a promising method for enhancing radiotherapy effectiveness. Moreover, CAP exhibits selective properties, causing less damage to normal kidney cells compared to cancer cells under the same conditions.

**Keywords:** Cold Atmospheric Plasma, Radiosensitizer

### ■ Radiosensitizing Effect of Green Synthesis ZnO Nanoparticles on Ferroptosis in Triple Negative Breast Cancer Cells (MDA-MB453)

Mina Pourhabib Mamaghani <sup>1,\*</sup>, Hosein Azimian <sup>1</sup>

<sup>1</sup>Medical Physics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Medical Physics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. Email: pourhabibM4001@mums.ac.ir

#### Abstract

**Background:** Triple-negative breast cancer (TNBC) is aggressive and resistant to treatment, highlighting the need for new therapies such as ferroptosis. This study aimed to investigate the effects of green-synthesized zinc oxide nanoparticles (ZnO NPs) on the MDA-MB-453 cell line and their potential to induce ferroptosis.

**Materials and Methods:** ZnO NPs were synthesized using *Nymphaea alba* and characterized. The MDA-MB-453 cells were treated with zinc oxide nanoparticles to assess toxicity and determine the half-maximal inhibitory concentration (IC50). Levels of malondialdehyde (MDA) and glutathione peroxidase (GPX), key markers of ferroptosis, were measured.

**Results and Conclusions:** Our investigations have demonstrated that: (1) cell death induced by ZnO NPs is attributable to ferroptosis; (2) ferroptosis resulting from ZnO NPs is associated with increased lipid peroxidation and decreased GPX levels. We hypothesize that ZnO NPs may reduce cancer cell resistance by acting as radiosensitizing agents through the induction of ferroptosis. Key aspects of ZnO nanoparticles include their synthesis via the sol-gel method, green synthesis, selective function, and potential as radiosensitizing agents.

**Keywords:** ZnO Nanoparticles, Radiosensitizer, Triple Negative Breast Cancer

### ■ Evaluating the Impact of *Toxoplasma gondii*-Derived Recombinant Protein (rGRA6Nt) on Radiosensitivity and Colony Formation in 4T1 Breast Cancer Cells

Mohammad Sobhan Mokhtari Zamenjani <sup>1,\*</sup>, Saba ordibehehti <sup>2</sup>

<sup>1</sup>Department of Parasitology and Mycology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Department of Medical Physics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Department of Parasitology and Mycology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: sobhan.mokhtary@gmail.com

#### Abstract

**Background:** Radiation therapy is a cornerstone of cancer treatment, yet the development of resistance remains a significant challenge. This study investigates the effects of *Toxoplasma gondii*-derived recombinant protein (rGRA6Nt) on the radiosensitivity and colony formation ability of 4T1 breast cancer cells. We hypothesized that rGRA6Nt would enhance the susceptibility of 4T1 cells to radiation and reduce their clonogenic potential. The findings highlight the potential of rGRA6Nt as a novel adjuvant to improve radiotherapy outcomes.

**Materials:** -4T1 breast cancer cell line

- *Toxoplasma gondii*-derived recombinant protein (rGRA6Nt)

- Radiation source for radiosensitivity testing

- Standard laboratory equipment for cell culture and clo-

nogenic assays

**Methods:** 1. Cell treatment: 4T1 cells were cultured and treated with rGRA6Nt at concentrations of 10, 20, and 40 µg/mL for 24 hours.

2. Colony formation assay: Treated and untreated 4T1 cells were seeded in 6-well plates (100 cells/well) and cultured for 10 days. Colonies were fixed, stained with crystal violet, and counted to assess the impact of rGRA6Nt on clonogenic potential.

3. MTT assay: The cytotoxic effects of rGRA6Nt on 4T1 cells were evaluated using the MTT assay. Cells were seeded at a density of  $5 \times 10^3$  cells/well in 96-well plates and treated with rGRA6Nt at concentrations of 10, 20, and 40 µg/mL for 24 hours. Subsequently, 20 µL of MTT reagent (5 mg/mL) was added to each well and incubated for 4 hours at 37°C. The formazan crystals were dissolved in 100 µL of dimethyl sulfoxide (DMSO), and absorbance was measured at 570 nm using a microplate reader. Cell viability was calculated as a percentage relative to untreated controls.

4. Radiosensitivity test: After treatment with rGRA6Nt, 4T1 cells were irradiated at doses of 0, 2, 4, and 6 Gy. Surviving colonies were quantified to calculate the surviving fraction and determine the effect of rGRA6Nt on radiosensitivity.

5. Statistical analysis: Data were analyzed using one-way ANOVA, with  $P < 0.05$  considered statistically significant.

**Results:** 1. Colony formation assay: Treatment with rGRA6Nt significantly reduced the colony-forming ability of 4T1 cells in a dose-dependent manner. At 40 µg/mL, colony numbers decreased by 70% compared to untreated controls ( $P < 0.05$ ).

2. Radiosensitivity test: Pre-treatment with rGRA6Nt enhanced the radiosensitivity of 4T1 cells. At 6 Gy, the surviving fraction was reduced by 40% in cells treated with 20 µg/mL of rGRA6Nt compared to irradiated controls without treatment ( $P < 0.01$ ). This suggests that rGRA6Nt sensitizes cancer cells to radiation, potentially improving therapeutic efficacy.

3. MTT assay: The MTT assay revealed a cytotoxic effect of rGRA6Nt on 4T1 cells at lower concentrations, while no significant lethality was observed at 40 µg/mL. At 45 and 50 µg/mL, cell viability decreased by 10% and 25%, respectively, compared to untreated controls ( $P < 0.05$ ). However, at 40 µg/mL, cell viability remained comparable to untreated controls, indicating that this concentration does not exert a lethal effect. These results suggest that while rGRA6Nt can reduce cell viability at certain doses, its impact at higher concentrations may plateau.

**Conclusions:** The results demonstrate that rGRA6Nt effectively reduces the clonogenic potential of 4T1 breast cancer cells and enhances their radiosensitivity. These findings support the potential application of rGRA6Nt as a radiosensitizer in cancer treatment. Future studies should explore the underlying mechanisms of these effects and evaluate the efficacy of rGRA6Nt in combination with standard radiotherapy protocols.

**Keywords:** Toxoplasma gondii, rGRA6Nt, 4T1 Breast Can-

cer Cells, Radiosensitivity, Colony Formation

## ■ Induction of Necroptosis with Selenium Nanoparticles and Analysis of Radiosensitivity in HT29 Cells

Saba Ordibeheshti<sup>1</sup>, Mohammad sobhan Mokhtari Zamenjani<sup>1</sup>

<sup>1</sup>Department of Medical physics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Department of Parasitology and Mycology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\* Corresponding Author: Department of Medical physics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: sabaordibeheshti2001@gmail.com

### Abstract

**Background:** Necroptosis has gained significant interest due to its potential as an exploitable therapeutic target in cancer treatment. The redox activity and cytotoxic selectivity of selenium nanoparticles (SeNPs) make them promising candidates as anticancer agents. This study describes the induction of necroptosis in HT29 colorectal cancer cells caused by SeNPs and examines the combined influence of SeNPs and ionizing radiation on the radiosensitivity of the cancer cells.

**Methods:** The cytotoxic effects of SeNPs on HT29 cells were determined by culturing the cells in the presence of SeNPs at various concentrations and subjecting them to the MTT assay. Apoptosis, necroptosis, and necrosis were assessed by Annexin V/PI flow cytometry analysis to analyze the cellular death pathways. A colony survival assay was conducted to determine the ability of cells to proliferate and their susceptibility to radiation after exposure to SeNPs. Cells were exposed to ionizing radiation with or without prior treatment with SeNPs to assess changes in cytotoxicity.

**Results:** This research investigated the cytotoxicity and radiosensitizing potential of SeNPs on HT29 colon carcinoma cells. An IC50 value of approximately 2 µg/mL was established during MTT assays, with a gradual decrease in cell viability observed as the concentration increased. Flow cytometry results showed that SeNPs treatment resulted in a considerable induction of necroptosis, evidenced by the ability of the specific necroptosis inhibitor, necrostatin-1, to inhibit this effect. In colony formation assays, SeNPs alone and in combination with radiation reduced colony formation in treated cells, with the combination providing added benefits. SeNPs also enhanced the effectiveness of ionizing radiation, with an enhancement ratio of 1.6 for DNA damage. Collectively, these results reveal SeNPs as promising candidates for further studies in colon cancer-targeted therapies.

**Conclusions:** The present study shows that SeNPs induce necroptosis in HT29 cells and increase their radiosensitivity, suggesting their potential as radiosensitizers in colorectal cancer treatment. Based on these outcomes, the potential synergism between SeNPs

and radiotherapy might enhance the killing effect on tumor cells through an understanding of necroptosis as a mechanism for cancer cell elimination. **Keywords:** Necroptosis, Radiosensitivity, Selenium Nanoparticles

### ■ A Novel Strategy to Enhance Prostate Cancer Radiosensitization using Quercetin Conjugated Nanosystems

Parisa Rouhbakhsh Azimi <sup>1</sup>, Amir Danyaei, Mahmoud Gharbavi <sup>2</sup>

<sup>1</sup>Department of Medical Physics, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

<sup>2</sup>Nanotechnology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

\* *Corresponding Author:* Department of Medical Physics, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: Parisa.azimi0922@gmail.com

#### Abstract

**Background:** Prostate cancer is a leading cause of cancer-related mortality among men. While radiotherapy is a critical component in the treatment of prostate cancer, radioresistance remains a significant therapeutic challenge. Selenium nanoparticles are recognized for their radiosensitizing properties. Their combination with quercetin may enhance radiotherapy efficacy by improving bioavailability and inhibiting DNA repair in cancer cells.

**Methods:** Albumin-coated selenium nanoparticles were synthesized, followed by the conjugation of quercetin as a pharmacologically active agent. The physicochemical properties of the nanostructures were characterized using dynamic light scattering (DLS) and UV-visible spectroscopy. The synergistic effects on LNCaP cell lines were assessed through cell viability assays, both with and without radiation exposure.

**Results:** The DLS measurements indicated the size, shape, and stability of the nanoparticles, while UV-visible spectroscopy confirmed the successful synthesis and interaction between selenium and the drug. In cellular studies, the nanoparticles reduced LNCaP cell viability when exposed to 2 Gy of radiation. The quercetin-conjugated nanoparticles were the most effective, demonstrating dose-dependent cytotoxicity. Their cytotoxicity increased with 2 Gy X-ray irradiation, underscoring their potential to enhance radiotherapy efficacy.

**Conclusions:** This study demonstrates that the nanosystems, due to their favorable physicochemical properties and significant cytotoxic effects, can substantially increase the radiosensitivity of LNCaP prostate cancer cells. The combination of these nanoparticles with a 2 Gy dose resulted in a synergistic reduction in cell viability, indicating a high potential for improving radiotherapy effectiveness.

**Keywords:** Nanosystems, Radiosensitivity, Quercetin

### ■ The Association Between Dietary Acid Load, Alkaline Water and Cancer Incidence: A Systematic Review

Arian Bandari <sup>1, \*</sup>, Sajad Mirzaei <sup>2</sup>, Vahideh Aghamohammadi <sup>3</sup>, Aynaz Mohammadian <sup>1</sup>

<sup>1</sup>Student Research Committee, Khalkhal University of Medical Sciences, Khalkhal, Iran

<sup>2</sup>Founder of Cancer Cancel (Saratano) Medical Startup, Tehran, Iran

<sup>3</sup>Department of Nutrition, Khalkhal University of Medical Science, Khalkhal, Iran

\* *Corresponding Author:* Student Research Committee, Khalkhal University of Medical Sciences, Khalkhal, Iran. Email: arianbandari8282@gmail.com

#### Abstract

**Background:** Dietary acid load (DAL) and alkaline water have garnered attention for their potential roles in cancer prevention and treatment. The acid-base balance hypothesis suggests that a diet high in acid-forming foods and beverages may create a pro-inflammatory environment conducive to cancer development, while alkaline water and alkaline-forming diets could counteract these effects. Despite growing public and scientific interest, the association between DAL, alkaline water, and cancer risk or progression remains inconclusive. This review aimed to clarify the association between DAL, alkaline water, and cancer incidence.

**Methods:** This systematic review was conducted according to the PRISMA protocol. A comprehensive literature search was performed across PubMed, Web of Science, Scopus, and Embase databases from inception to October 2023. Studies were included based on predefined criteria: (1) peer-reviewed articles, (2) human studies, (3) assessment of dietary acid load or alkaline water, and (4) cancer-related outcomes. Exclusion criteria included animal studies, reviews, commentaries, and insufficient data on DAL or alkaline water. Data extraction and quality assessment were performed independently by two reviewers using the Newcastle-Ottawa Scale for observational studies and the cochrane risk of bias tool for clinical trials. Disagreements were resolved through consensus. Key outcomes included cancer incidence, survival rates, tumor progression, and biomarkers of inflammation and oxidative stress. A meta-analysis was performed where data allowed, using a random-effects model to account for heterogeneity.

**Results:** Out of 3,412 initial records, 47 studies met the inclusion criteria, comprising 32 observational studies and 15 interventional trials. Dietary acid load, assessed by indices such as potential renal acid load (PRAL) and net endogenous acid production (NEAP), was positively associated with cancer risk, particularly for colorectal, breast, and prostate cancers. High DAL was linked to increased levels of pro-inflammatory markers (e.g., C-reactive protein, interleukin-6) and oxidative stress. Conversely, alkaline water consumption demonstrated potential benefits in reducing oxidative stress and improving hydration status in cancer patients, although evidence was limited by small sample sizes and methodological heterogeneity.

ity. Studies on alkaline diets and cancer outcomes were inconsistent, with some reporting reduced tumor progression and others showing no significant effect. Meta-analysis revealed a pooled relative risk (RR) of 1.22 (95% CI: 1.08 - 1.37) for high DAL and cancer incidence, while data on alkaline water were insufficient for quantitative synthesis.

**Conclusions:** This systematic review suggests a modest positive association between high dietary acid load and cancer risk, likely mediated by inflammatory and oxidative stress pathways. Alkaline water shows potential as a supportive therapy for cancer patients, but evidence remains inconclusive due to limited high-quality trials. Future research should focus on large-scale, well-designed prospective studies and randomized controlled trials to clarify the mechanisms and clinical relevance of dietary acid load and alkaline water in cancer prevention and management.

**Keywords:** Dietary Acid Load, Alkaline Water, Cancer, Inflammation, Oxidative Stress, PRISMA, Systematic Review, Meta-analysis

### ■ In Vitro Study of the Effect of Intraoperative Radiotherapy of Breast Cancer on the Microenvironment and Phenotype of Cancer Cell

Sima Sayah<sup>1</sup>, Fahimeh Hosein-beige<sup>2</sup>, Soheila Sharifian-jazi<sup>2,3</sup>, Hamed Zamani<sup>2,3</sup>, \*

<sup>1</sup>Department of Radiology, Feroz Educational Hospital, North Khorasan University of Medical Sciences, North Khorasan, Iran

<sup>2</sup>Department of Radiology, Manzariyeh Educational Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>3</sup>Department of Medical Physics, Faculty of Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran

\* Corresponding Author: hamed9243483@gmail.com

#### Abstract

**Background:** Intraoperative radiotherapy (IORT) is a high-dose treatment method administered in a single fraction during surgery. Surgery and radiation induce changes in the tumor microenvironment by altering cytokines. This study aimed to determine the effects of changes caused by surgery and IORT on the breast tumor microenvironment or bed, specifically on the growth and motility of MCF-7 cells, and to evaluate the effectiveness of the drug Aurapten.

**Methods:** Samples were collected from 37 patients undergoing breast surgery. Peripheral blood serum (PS) samples were taken from each patient before surgery, and wound fluid (WF) samples were collected 24 hours after surgery. Patients were divided into two groups: (1) those who underwent IORT treatment after surgery (IORT+), and (2) those who underwent surgery only (IORT-). The effectiveness of the collected serums on the growth and survival of MCF-7 cells was investigated using the MTT assay and three-dimensional culture. The effect on the motility of MCF-7 cells was examined using the

wound healing test.

**Results:** The results indicated that radiotherapy increased the growth of cells receiving serums. Cells treated with WF+ formed larger colonies than those that received WF-. However, the motility of the group that received WF+ was significantly lower than that of the group that received WF- (P = 0.02). The results also demonstrated that Aurapten has a cytotoxic effect on MCF-7 cells, with increased drug concentration and duration of exposure enhancing the lethal effect.

**Conclusions:** This study showed that radiotherapy during surgery does not reduce the growth of cancer cells but does decrease their motility. The use of Aurapten can reduce breast tumor cells.

**Keywords:** Intraoperative Radiotherapy, MTT Test, 3D Culture, Wound-Healing Test, Wound Fluid, Aurapten, Breast Cancer

### ■ Assessment of Radiation Dose and Radiation-Induced Cancer Risk in Ho-166 and Y-90 Radioembolization

Asra Sadat Talebi<sup>1,\*</sup>, Roghiyeh bodaghi<sup>2</sup>

<sup>1</sup>Department of Medical Physics, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Department of Medical Physics, Tarbiat Modares University, Tehran, Iran

\* Corresponding Author: Department of Medical Physics, Tabriz University of Medical Sciences, Tabriz, Iran. Email: Asra.talebi@yahoo.com

#### Abstract

**Background:** Transarterial radioembolization (TARE) serves as a palliative measure for both primary and metastatic liver malignancies. This minimally invasive procedure delivers radiation directly to the tumor via tiny radioactive beads, offering symptom relief and potentially slowing disease progression. Currently, Y-90 and Ho-166 are utilized in TARE, representing two key radioactive isotopes employed for this procedure. This study aims to evaluate and compare the radiation doses as well as the associated risks of cancer induction between Y-90 and Ho-166 TARE.

**Methods:** The study utilized Gate 9.2 Monte Carlo toolkit in conjunction with ICRP110 voxelized phantom. A tumor with a diameter of 3 cm was modelled within the liver, with Y-90 and Ho-166 uniformly distributed within the tumor. Absorbed doses in phantom organs were calculated. Employing the biological effects of ionizing radiation (BEIR VII) report, the lifetime attributable risk (LAR) of cancer incidence and mortality was computed.

**Results:** In Y-90 TARE, the mean absorbed doses for tumoral liver tissue, non-tumoral liver tissue, stomach, lung and bladder are 3.36, 0.003,  $3.66 \times 10^{-6}$ ,  $5 \times 10^{-7}$  and 0.001 Gy/MBq, respectively. In Ho-166 TARE, these values for tumoral liver tissue, non-tumoral liver tissue, stomach, lung and bladder are 0.466, 0.271,  $2.46 \times 10^{-5}$ ,  $1.66 \times 10^{-5}$  and  $6.07 \times 10^{-5}$  Gy/MBq, respectively. The mean cancer incidence risks per 100,000 people were 1.5 and 10.2

for Y-90 TARE and Ho-166 TARE, respectively. For Y-90 TARE and Ho-166 TARE, the mean LAR of cancer mortality for all cancer was 0.52 and 3.36, respectively, per 100,000 people.

**Conclusions:** The radiation-induced cancer risk in Ho-166 TARE is significantly higher Y-90 TARE. Consequently, Ho-166 TARE is associated with a noteworthy risk of cancer induction, underscoring the importance of optimizing patient radiation doses to mitigate this risk.

**Keywords:** Radioembolization, Y-90, Ho-166, Monte Carlo, Lifetime Attributable Risk

### ■ Dosimetry in Ac-225 Targeted Alpha Particle Therapy Utilizing Cherenkov Luminescence Imaging

Asra Sadat Talebi <sup>1,\*</sup>, Roghiyeh Bodaghi <sup>2</sup>

<sup>1</sup>Department of Medical Physics, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Department of Medical Physics, Tarbiat Modares University, Tehran, Iran

\* *Corresponding Author:* Department of Medical Physics, Tabriz University of Medical Sciences, Tabriz, Iran. Email: Asra.talebi@yahoo.com

#### Abstract

**Background:** Osteosarcoma is an aggressive type of bone cancer characterized by the formation of osteoid tissue and the widespread presence of insulin-like growth factor 1 receptor (IGF1R), with some cases also expressing human epidermal growth factor receptor 2 (HER-2). These features create potential for utilizing alpha particle-emitting isotopes for targeted radiation therapy, specifically targeting bone-forming tumors and metastases expressing IGF1R or HER-2. Actinium-225 (Ac-225) is one of the alpha-emitting radionuclides commonly used in the treatment of osteosarcoma. Due to the short-range and high-energy deposition characteristics of alpha particles, it is crucial to gather precise data on dose distribution to optimize the effectiveness of this therapeutic method. Utilizing current individual dosimetry techniques, such as single-photon emission computerized tomography (SPECT) and positron emission tomography (PET) image-based dosimetry, in targeted alpha therapy (TAT) encounters significant challenges and, at times, proves impractical. Hence, there is a pressing need to investigate alternative dosimetry approaches, such as Cherenkov luminescence image-based dosimetry.

**Methods:** The Monte Carlo codes GATE (version 9.2) were utilized to simulate post-TAT Cherenkov luminescence imaging (CLI) in the MOBY mouse phantom. A tumor, with a diameter of 5 mm, was modeled within the femur, with Ac-225 uniformly distributed within the tumor. Personalized dosimetry accuracy was assessed by estimating the root mean square errors (RMSEs) between the acquired image-based dose volume histograms (DVHs) and the reference DVHs.

**Results:** The in-silico results demonstrated that the RMSE value is less than 1, indicating high accuracy. Additionally,

our analysis revealed that the distribution of Cherenkov radiation closely aligns with the absorbed dose distribution within the tumor.

**Conclusions:** Our findings suggest that Cherenkov emission holds promise for individual dosimetry in TAT. Cherenkov luminescence image-based dosimetry proves to be easily applicable in preclinical investigations, distinguished by its simplicity and effectiveness.

**Keywords:** Targeted Alpha Particle Therapy, Dosimetry, Cherenkov Luminescence Imaging

### ■ The Effects of Ginseng Extract and Its Compounds on Radiation Exposure: A Systematic Review

Arian Bandari <sup>1,\*</sup>, Sajad Mirzaei <sup>2</sup>, Vahideh Aghamohammadi <sup>3</sup>, Aynaz Mohammadian <sup>1</sup>

<sup>1</sup>Student Research Committee, Khalkhal University of Medical Sciences, Khalkhal, Iran

<sup>2</sup>Founder of Cancer Cancel (Saratano) Medical Startup, Tehran, Iran

<sup>3</sup>Assistant Professor, Department of Nutrition, Khalkhal University of Medical Science, Khalkhal, Iran

\* *Corresponding Author:* Student Research Committee, Khalkhal University of Medical Sciences, Khalkhal, Iran. Email: arianbandari8282@gmail.com

#### Abstract

**Background:** Ionizing radiation can induce cellular damage, oxidative stress, and inflammation, leading to significant health risks. Ginseng, a traditional herbal remedy with antioxidant and anti-inflammatory properties, has been investigated for its potential radioprotective effects. This systematic review evaluates the effects of ginseng extract and its active compounds on radiation exposure outcomes, following the PRISMA (preferred reporting items for systematic reviews and meta-analyses) protocol.

**Methods:** A comprehensive literature search was conducted across multiple databases, including PubMed, Scopus, Web of Science, and Cochrane Library, from inception to December 2024. Studies were included if they investigated the effects of ginseng or its bioactive compounds, such as ginsenosides, on radiation-induced damage in cellular, animal, or human models. Articles were screened and selected by two independent reviewers, with discrepancies resolved by a third reviewer. Data extraction focused on study design, intervention characteristics, radiation dose and type, outcomes measured, and findings. Risk of bias was assessed using the Cochrane risk-of-bias tool for randomized studies and SYRCLE's tool for animal studies. Narrative synthesis and meta-analysis were performed when appropriate.

**Results:** Out of 2,347 articles identified, 62 studies met the inclusion criteria, comprising 38 animal studies, 15 in vitro studies, and 9 human trials. Ginseng extract and ginsenosides demonstrated significant radioprotective effects, including reduced oxidative stress markers, enhanced DNA repair mechanisms, and mitigation of radiation-induced inflammation. Key bioactive compounds, such as Rg1, Rb1, and Rd, were particularly effective in

decreasing reactive oxygen species (ROS) levels and improving cell viability post-radiation. Human studies reported improvements in hematological parameters and reduced radiation-related side effects, with minimal adverse events. However, variability in dosages, formulations, and study designs limited direct comparability. Meta-analysis of 20 studies showed a pooled relative risk reduction of radiation-induced damage by 42% (RR: 0.58; 95% CI: 0.46 - 0.72;  $P < 0.001$ ).

**Conclusions:** Ginseng extract and its compounds show promising radioprotective effects across preclinical and clinical studies, potentially attributable to their antioxidant and anti-inflammatory properties. However, heterogeneity in study methodologies highlights the need for standardized clinical trials to determine optimal dosages and formulations for effective use. Future research should also explore the molecular mechanisms underlying these effects and evaluate long-term outcomes.

**Keywords:** Ginseng, Ginsenosides, Radioprotection, Ionizing Radiation, Systematic Review, PRISMA Protocol

### ■ Investigation and Structural Study of SnO<sub>2</sub> Nanocomposite Based on Polyvinyl Chloride for Protection Against X-rays

Milad Amiri <sup>1,\*</sup>, Ehsan Ebrahimi <sup>1</sup>, Hamid Gholamhosseinian <sup>2</sup>

<sup>1</sup>Faculty of Physics and Nuclear Engineering, Shahrood University of Technology, Shahrood, Iran

<sup>2</sup>Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

\*Corresponding Author: Faculty of Physics and Nuclear Engineering, Shahrood University of Technology, Shahrood, Iran. Email: miladamiri991376@gmail.com

#### Abstract

**Background:** This study addresses the need to replace

lead-based shields due to their toxicity and weight, proposing alternatives such as polymer nanocomposites with nanofillers (e.g., bismuth, gadolinium), barium-based bioactive glasses, and epoxy composites enhanced with graphene oxide and lead oxide. These materials offer improved radiation absorption, biocompatibility, and reduced secondary radiation, particularly with the incorporation of titanium/bismuth multilayered nanoparticles and SnO<sub>2</sub>, which enhance glass/PVC composites. These innovations provide lightweight, eco-friendly radiation protection for medical and industrial applications.

**Methods:** Nanocomposites of polyvinyl chloride (PVC) and SnO<sub>2</sub> were synthesized using the solution casting method, with weight percentages calculated using Equation 1. Structural properties were analyzed using X-ray diffraction (XRD), and mechanical performance was evaluated through tensile strength testing. Radiation protection was assessed using an Am-241 radioactive source and a Siemens CT-simulation device's X-ray tube.

$$Wt\%SnO_2 = \frac{Weight\ of\ SnO_2}{Weight\ of\ PVC + Weight\ of\ SnO_2} 100$$

**Results:** Results showed that pure PVC has an amorphous structure with low crystallinity, while SnO<sub>2</sub>-PVC composites (20%, 40%, and 60%) exhibited crystalline structures, with the 40% composition being fully crystalline. Tensile strength increased with SnO<sub>2</sub> incorporation, from 0.299 (pure PVC) to 0.391 (60% SnO<sub>2</sub>), though gains beyond 20% were minimal. Radiation attenuation tests revealed that SnO<sub>2</sub> significantly reduced the material thickness needed to match lead's performance. For instance, 60% SnO<sub>2</sub> required only 0.018 cm, outperforming lead by 28%. These findings demonstrate the potential of SnO<sub>2</sub>-PVC composites as effective, lightweight alternatives to traditional lead shielding.

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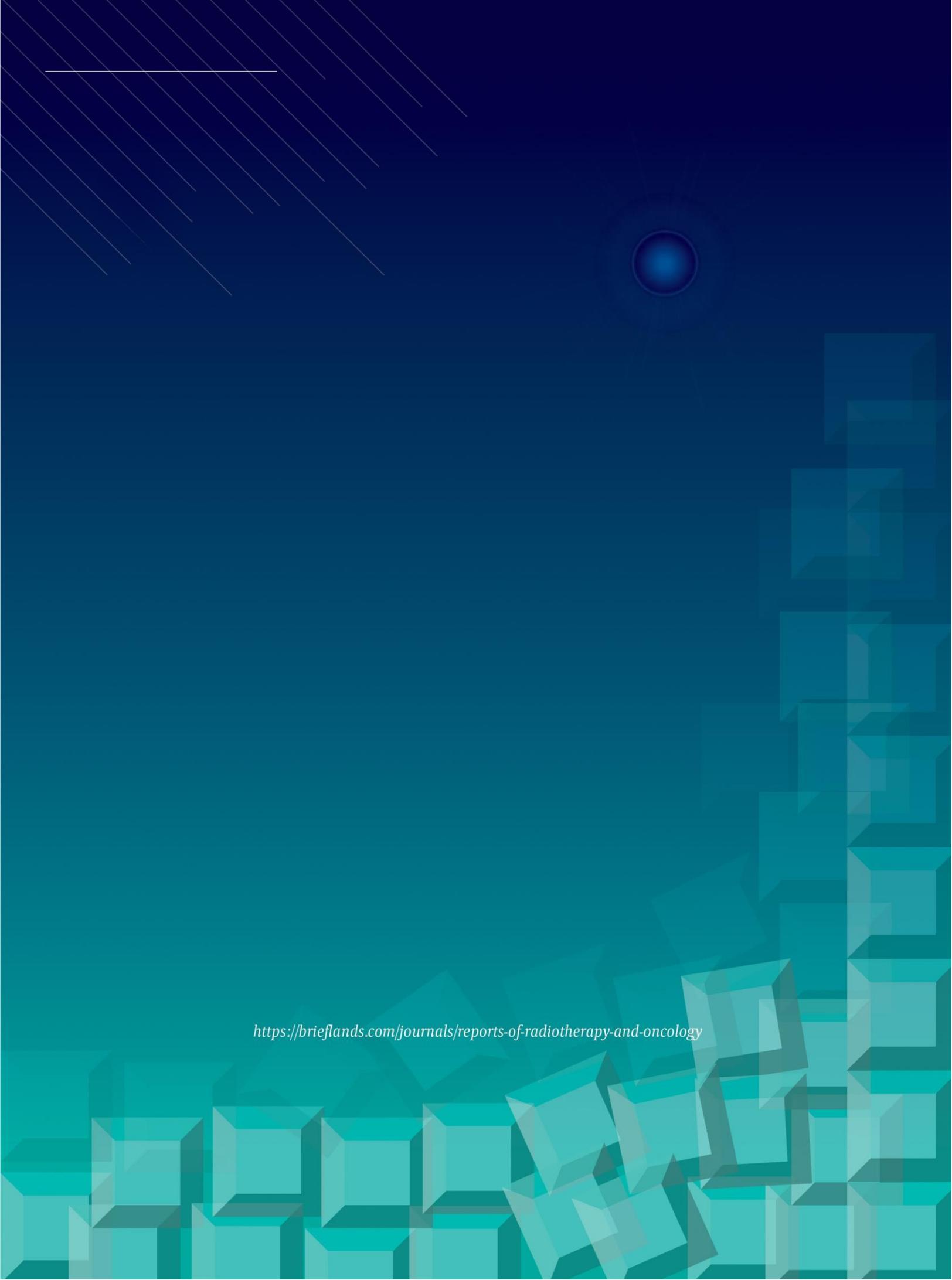
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