Reports of Radiotherapy & Oncology

Official journal of Iranian Society of Clinical Oncology

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Reports of Radiation and Oncology (RRO) is an international, specialized, peer- reviewed journal in all areas of oncology. The journal welcomes the submission of manuscripts that meet the general criteria of significance and scientific excellence in all fields of cancer, and will publish:

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REFERENCES

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Ford MJ, Munro JF. Introduction to Clinical Examination. 7th ed. Edinburgh: Churchill Livingstone; 2000.

If only a part is cited, add the page numbers, and volume number in the case of multi-volume works, at the end of the reference.

Meltzer PS, Kallioniemi A, Trent JM. Chromosome Alterations in Human Solid Tumors. In: Vogelstein B, Kinzler KW, editors. The Genetic Basis of Human Cancer. New York: McGraw-Hill; 2002. p. 93-113.

If you need to reference a book written by more than six authors, list the first six authors' names followed by "et al" thus:

Cohen J, Brown A, Smith B, Jones G, Murphy M, McKay P et al.

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Meydani SN, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF, et al. Vitamin E and Respiratory Tract Iinfections in Elderly Nursing Home Residents: a Randomized Controlled Trial. JAMA. 2004 Aug 18;292(7):828-36.

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Royal College of General Practitioners. The Primary Health Care Team. RCGP website 2003 [cited 2004 Sep 22]; Available from: URL: http://www.rcgp.

CONTENTS

CONTENTS

CONTENTS

CONTENTS

■ Evaluation of the Variability of Depth of Supraclavicular and Axillary Lymph Nodes in Patients With Breast Cancer and its Role in Radiotherapy Treatment Planning

Ahmad R Mafi[1*], Robab Anbiaee[2], Ahmad Ameri[2], Khosro M Sheibani[1]

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Abstract

Aim: Breast cancer is the most common malignancy among females worldwide. Radiation is used to treat patients at high risk for microscopic residual disease of the supraclavicular and axillary level III lymph nodes. Traditionally, supraclavicular area is treated by a single anterior field with a prescribed dose at 3-cm depth. However, uniform dosing to the depth of 3 cm is of great concern. The current study aimed at measuring the certain depth of supraclavicular and axillary level III nodal groups, and finding a relation between the body mass index (BMI) and the measured depths.

Material and Methods: In 35 patients undergoing computed tomography (CT) scanning in treatment position, the minimum and maximum depths of supraclavicular and axillary level III lymph nodes were measured on CT images. The relation between the depth of doses and patents' BMI was determined.

Results: All patients had maximum supraclavicular depth of <38.8 mm. The depth of axillary level III lymph nodes, however, was significantly different between the patients with BMI $\geq$30 kg/m^{2} and the ones with BMI <30 kg/m^{2}. In majority of the patients, prescribing the depth dose of 3 cm resulted in the underdosage of the lymph nodes.

Conclusion: The traditional method of radiation at the depth dose of 3 cm did not optimally cover the axillary level III nodes. In overcrowded medical centers, considering such depth doses may give an adequate coverage in >90% of the cases. The depth doses of 47, 53, and 60 mm are suggested for patients with BMI $\leq$24.9, 25-29.9, and $\geq$30 kg/m2, respectively.

Keywords: Axillary Lymph Nodes; Breast Cancer, Radiotherapy; Supraclavicular Lymph Nodes

■ The 2D-Dose Reconstruction by Artificial Neural Network for Pretreatment Verification of IMRT Fields

Seied Rabie Mahdavi[1], Mohsen Bakhshandeh[2], Aram Rostami[3*], Ali Jabbari Arfaie[4]

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Abstract:

Purpose: The use of intensity modulated radiation therapy (IMRT) is rapidly developing in clinical settings. Because of the high complexity and uniqueness of IMRT treatment plans, patient-specific pretreatment quality assurance (QA) is generally considered as a necessary prerequisite for patients. The current study aimed at proposing a new methodology of electronic portal imaging device (EPID)-based dose validation for the pretreatment verification of IMRT fields by applying artificial neural networks (ANNs).

Methods: The ANN should be trained and validated before using for pretreatment dose verification. For this purpose, 20 EPID fluence maps of anterior-posterior (AP) prostate IMRT field were used as an input for ANN (feed forward type) as well as a dose map of the fluence maps predicted by TPS as an output for ANN.

Results: After the training and validation of the neural network, the analysis of 10 IMRT prostate AP fields showed excellent agreement between ANN output and dose map predicted by TPS. The average overall field pass rate was 96.0% ± 0.1% with 3mm/3% criteria.

Conclusion: The results indicated that the ANN can be used as a cost-effective, rapid, and powerful tool for pretreatment dose verification, based on an EPID fluence map.

Keywords: Artificial Neural Network; Electronic Portal Imaging Device; Dose Verification; Intensity Modulated Radiation Therapy

■ The Clinical Application of Hyperthermia as a Potent and Synergistic Effect of Enhancer for Radiation Therapy: A Review Study

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Abstract:

Background: Hyperthermia (HT) was used in clinical practices since 1995 BC, the time of ancient Egypt. The term of HT means increasing the tumor temperature from 38°C to 43°C. HT is most often used in combination with other modalities such as radiation therapy (RT) and/or chemotherapy (CT). There are 3 types of HT in cancer treatment, including local, regional, and whole-body.

Method and Materials: Today, HT may be used before, after, or during the RT depending on the type of cancer. In spite of many studies conducted in this regard, the exact mechanism of direct HT is not well understood .Certainly, therapeutic effects of HT mostly rely on its combination with other modalities in cancer treatment; it is also remarkable that the HT can sensitize tumor cells to other forms of therapy; i e, RT. The radiosensitizer effect of HT is the main factor for its synergistic effects in combination with radiation; hence, HT plus RT is known as an immunotherapy method in cancer treatment. Also, HT can increase perfusion to tumors, make them more sensitive to RT, and increase cell-killing rate. Briefly, another effect of heating tumors after the radiation is to prohibit the DNA/RNA repair mechanisms through the synthesis of heat shock proteins (HSPs). TER is a factor to determine the synergistic effects of HT plus RT, which relates to the interaction between RT and HT, and is defined as the level of x-ray doses required to produce a given level of biologic damage with and without the application of heat. TER ranges about 1.5 for several human tumor types.

Result: A large number of studies indicated the clinical effectiveness of HT plus RT in vivo and/or in vitro. Regardless of the results of many studies, the exact mechanism of HT plus RT remains unclear so far. A randomized clinical trial reported that the CR rate 68.5% for HT plus RT and 23.5 % for radiotherapy alone. Several phase III clinical trials were performed on HT plus RT. A recently conducted clinical trial in the School of Medicine at Duke University, randomized patients into 2 groups of RT plus HT and, RT alone; patients with breast, head & neck, melanomas, and other regions tumors comprised 64%,13%, 10%, and 12% of the study population, respectively. The Dutch deep hyperthermia compared the RT alone with RT + HT and demonstrated the cost-effectiveness of HT. In the current study, a total of 363 patients with locally advanced pelvic tumors were explored in a 12-year follow- up period. Local control with HT+RT was 56% vs. 37% for RT alone (P=0.01), and survival rate was also higher in the HT+RT (37%) than the RT alone (20%) groups (P=0.03). Another study on 11 patients with recurrent esophageal cancer confirmed the efficacy of HT.

Conclusion: In conclusion, based on the results of clinical trials on the effectiveness of HT in human cancer, HT can improve the output of radiation therapy, optimize RT to increase tumor control probability, and reduce normal tissue complication through the role of radiosensitizer and enhanced effects of radiation.

Keywords: Hyperthermia; Radiotherapy; Synergistic Effects

■ **DOI:XXXXXXX**

■ PNU-74654 Synergistically Enhances the Antiproliferative Activity of Gemcitabine via Targeting the Wnt/β-catenin Signaling Pathway in Pancreatic Cancer

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Abstract

Background: The Wnt/β-catenin pathway is one of the main dysregulated pathways in several malignancies including pancreatic cancer (PC). The current study aimed at exploring the anticancer activity of PNU-74654, as a Wnt/ β-catenin inhibitor, in PC cells alone and in combination with gemcitabine in 2- and 3-dimensional (2D and 3D) cell culture models in order to develop novel treatment strategies interfering with the Wnt/β-catenin pathway.

Methods: The viability of PC cells was determined using MTT assay, while the cytotoxicity of this agent was evaluated in a 3-D cell culture model (spheroid). Also, cell migration and invasion assays were studied. The expression levels of the candidate genes involved in cell cycle and migration, as well as the markers of Wnt/b-catenin pathway were evaluated at mRNA and/or protein levels by the reverse transcription polymerase chain reaction (RT-PCR) or the Western blotting techniques.

Results: PNU-74654 suppressed cell growth at IC50 value of 122 ± 0.4 μM/L and synergistically enhanced the antiproliferative activity of gemcitabine via the modulation of the Wnt pathway. PNU-74654/gemcitabine combination could reduce the migratory and invasiveness of PC cells, compared with the control cells through perturbation of E-cadherin.

Conclusion: The current study demonstrated the antitumor activity of PNU-74654 in PC supporting further investigations on the therapeutic potential of this novel anticancer agent in in vivo models.

Keywords: Pancreatic Cancer; PNU-74654; Wnt Pathway; Gemcitabine

■ **DOI:XXXXXXX**

■ Comparison of Dose Calculation Algorithms in External Beam Photon Radiation Therapy in Thorax Region

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Abstract:

The most important goal of radiation therapy is to transfer doses of ionizing radiation to cancerous tissue and simultaneously protect healthy tissue surrounding the cancerous area. In 3D radiotherapy, due to the increased accuracy of the design application, radiotherapy is performed on the basis of patient's computed tomography (CT) scan before the onset of treatment. In radiotherapy, the accurate dose calculation by the treatment planning system is of great importance in order to control the tumor and maintain healthy tissue.

The current experimental study compared the accuracy of the treatment planning software with different dose calculation

algorithms in chest radiotherapy. In order to verify the validity of treatment planning systems and study the effect of computational algorithms on the calculation results, based on the international atomic energy agency TEC-DOC 1583 instruction, 8 specific tests were defined for each system.

In the correction base algorithms, the maximum error observed in the lung heterogeneity was up to 16% as well as 4.7% in the bone. In the model base algorithms, the maximum error observed in the lung and bone was 6% and 5.6%, respectively.

Most problems occur in time calculation in which computations are done within lung heterogeneities with low-density or within bone tissue with high-density at low depth. The total error in high-energy was more than that of low-energy. Therefore, it is suggested that the use of 3D treatment planning systems with the advanced Monte Carlo simulation algorithms, especially for calculation in high-density heterogeneities and high-energy photonides, should be prioritized in radiotherapy centers.

Keywords: Radiotherapy; Treatment Planning Algorithm; Tissue Equivalent Phantom; Absorption Dose

■ **Measuring and Comparing Eye Doses in Whole-brain Radiation Therapy in the Collimator Rotation and Shielding Methods**

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Abstract:

Introduction: Radiotherapy (radiation therapy) means the use of ionizing radiation in order to cure cancer. Brain tumor was one of the most common cancers during the past 3 decades. Radiotherapy is a local treatment. Cancer cells are more sensitive to radiotherapy than healthy cells; thus, most of them are eliminated. The major goal of treatment planning in radiation therapy is to transfer the required radiation dose from ionizing radiation source to the cancerous tissue and simultaneously protect healthy tissue surrounding the tumor, especially the organs sensitive to ionizing radiation. The radiation therapy of brain cancer due to its close proximity to at risk organs, such as eye and the lens is highly sensitive. If the dose absorbed by eye exceeds the authorized limits, the side-effects such as cataracts are inevitable.

According to the previous studies on the probability of cataract occurring in brain radiotherapy, the current study aimed at calculating and comparing the dose absorbed by eye lens in whole-brain radiotherapy by the 2 methods of the collimator rotation and shielding, with 3 dosimetric instruments, on human phantom and tissue equivalent pages. Further study was conducted using the 3-D treatment planning system.

Materials and Methods: In order to calculate the dose absorbed by eye in 2 methods of the collimator rotation and shielding, a 6 VM Linear Accelerator with 100 cGy on a phantom with 3 dosimeter devices of ionization chamber, thermoluminescent dosimeter (TLD), and gafchromic film was used.

Results: The dose received to the lens of each eye ranged 3.75 to 6.01 in the collimator rotation procedure with ionization chamber (ppc-40), 4.51 to 5.08 cGy in TLD, and 4.03 to 5.04 cGy in gafchromic film and the ion chamber; however, it was 6.35-9.55, 6.10-8.58, and 5.96-8.28 cGy, respectively using the shield method at a zero angle.

Conclusion: The results of the current study showed that the dose received to the eye lens, radiated by the ionizing chamber in the collimator rotation, was 2.2% lower than that of the shielding method.

Keywords: Radiotherapy; Linear Accelerator; Eye; Shield; Treatment Planning; Cataract; Collimator

■ **Differentiation Between Benign and Malignant Lymph Nodes Using a Quantitative Analysis of Ultrasound Images**

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Abstract:

Objectives: Thyroid cancer is the most common endocrine malignancy with approximately 56,780 new cases reported in the United States in 2017. The surveillance, epidemiology, and end results (SEER) database reported that the incidence of thyroid cancer from 1975 to 2013 increased from 4.85 to 15.07 per 100,000 population. Advanced quantitative information, such as texture features, derived from ultrasound images can help for better diagnosis of lymph node cancer. The current study aimed at investigating the ability of texture analysis in differentiation between benign and malignant lymph nodes.

Methods: Twenty patients with benign and 20 patients with malignant lymph nodes approved by the fine needle aspiration biopsy were enrolled in the current study. Based on histograms, 9 parameters were extracted from each node: mean, variance, skewness, and kurtosis as well as percentiles 1% ,10%, 50% ,90% ,and 99% .Significant parameters were selected for further analyses and classifications .Finally ,benign and malignant lymph nodes were classified using the artificial neural network) ANN.(

Results : Results showed that kurtosis and percentiles 50% ,90%, and 99% were significantly different between benign and malignant lymph nodes) P values= 0.031 ,0.025 ,0.020 ,and 0.001, respectively .(Based on all significant parameters ,benign and malignant lymph nodes can be classified with 90% sensitivity, 95% specificity ,and 92.5% accuracy.

Conclusions :A quantitative analysis of ultrasound images can assist physicians to improve diagnostic accuracy and provide new insights into lesions .Texture parameters can be used as a prognostic biomarker in medical centers.

ABSTRACT

■ The Prevalence of *KRAS* Mutation in Colorectal Cancer Among Iranian Population: A Systematic Review and Meta-analysis Study

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Abstract

Background: Colorectal cancer (CRC) is one of the most common cancers worldwide and the *KRAS* mutations are a key factor in its progression. The current meta-analysis study aimed at evaluating the prevalence of *KRAS* mutations in patients with CRC in Iran.

Materials and Methods: Six online databases including PubMed, Science Direct, Scopus, Web of Science, Cochran Library, and Scientific Information Database (SID) were searched systematically up to January 2017. A random-effects meta-analysis was used to estimate the prevalence of *KRAS* mutations in patients with CRC by the event rate (ER) with 95% confidence interval (95%CI).

Results: Out of 82 articles extracted from the databases, 11 studies were enrolled in the current meta-analysis. The studies totally included 1814 patients with CRC and the mean age of 57.5 years. The pooled ER of the studies to estimate the prevalence of *KRAS* mutations in patients with CRC was 32.8% (95%CI=28.7%-37.3%). The pooled ER of the studies for the prevalence of codon 12 mutation was 72.5% (95%CI=59.8%-82.3%) and for codon 13 mutation was 20% (95%CI=14.6-26.7%).

Conclusions: The results showed that the prevalence of *KRAS* mutations in Iranian patients was different from those of many studies conducted in other countries; therefore, geographical region and race can affect the prevalence of *KRAS* mutations in patients with CRC. Also, codon 12 had the highest frequency among mutant codons, followed by codon 13 and glycine to aspartate and glycine to valine were the most prevalent mutations in codon 12.

Keyword: CRC*; Iran; KRAS;* Prevalence

Characteristics of the Studies Enrolled in the Current Meta-analysis Study

First Author (Year)	Province	Patients	Total KRAS Mutations	Mean Age	Gender (% Male)	Number of Mutant Codons	Number of Mutated Amino Acids in Codon 12*(N)
Bishehsari et al., 2006	Tehran	182	68	NA	57	12(45), 13(23)	Asp(16), Val(18), Cys(9), Ser(1), Ala(1)
Sobhani et al., 2010	Tehran	59	12	58	41.4	12(10), 13(2)	Asp(6), Ser(2), Val(2)
Shemirani et al., 2011	Tehran	48	6	NA	83	12(5), 13(1)	Asp(4), Cys (1)
Omidifar and Gerami-zadeh, 2015	Fars	100	32	59.1	55	12(24), 13(8)	Ala(12), Asp(9), Ser(1), Cys(1)
Amirifard et al., 2016	Kermanshah	33	11	51.5	78.8	12(10), 13(1)	Asp(5), Val(3), Ser(1), Cys(1)
Dolatkhah et al., 2016	East Azerbaijan	110	26	61.9	65	12(16), 13(9)	Asp(13), Val(2), Cys(1)
Koochak et al., 2016	Tehran	1000	336	55	57.3	12(286), 13(50)	Asp(137), Val(96), Ser(20), Ala(15), Cys(15), Arg(3)
Mohsen et al., 2016	South Khorasan	50	15	60.6	70	12(10), 13(4)	Asp(5), Val(5)
Payandeh et al., 2016	Kermanshah	83	37	57.7	61.4	12(30), 13(7)	Asp(12), Val(8), Ser(4), Ala(2), Cys(3), Arg(1)
Roudbari et al., 2016	Tehran	50	21	56.9	68	12(15), 13(6)	Asp(8), Val(3), Ser(2), Ala(1), Cys(1)
Vakil et al., 2016	Tehran	99	38	57	57.8	12(34), 13(4)	Asp(15), Ala(2), Cys(5), Ser(5), Val(7)

* **Mutation**: "Gly" to "other amino acids or mutant amino acid"

■ Development of Models for the Prediction of Pneumonitis Using Forward Variable Selection and LASSO Logistic Models for Patients With Breast Cancer Treated With 3D-CRT

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Abstract

Introduction: A part of lung is inevitably exposed to radiation in breast radiation therapy (RT). The current study aimed at developing a multiple logistic regression model as normal tissue complication probability model by the LASSO technique for patients with breast cancer treated with 3-dimensional cathode ray tube (3D-CRT) technique focusing on the changes of pulmonary function tests (PFTs) to achieve the optimal predictive parameters for the occurrence of symptomatic radiation pneumonitis and investigating the effects of dihydromyricetin (DMH) as input for the normal tissue complication probability (NTCP) models in comparison with dose-volume histogram (DVH).

Materials and method: Dosimetric and spirometry data of 51 patients with breast cancer were analyzed in the current study. The pulmonary function of the subjects were tested before RT, and 0, 3, and 6 months after the completion of RT. The relationship between dosimetric and clinical parameters of the patients was analyzed according to the univariate logistic regression, and the forward selection method was applied in the NTCP model to determine the risk factors affecting the obtained parameters.

Results: SRP was observed in 5 patients. Significant changes in pulmonary parameters were observed 3 and 4 months after RT in the study subjects. The bridge separation, central lung distance, and the mean irradiated lung volume in tangential field were 23.4 cm, 2.43 cm, and 10.06% in patients without pulmonary complication, respectively.

Conclusion: The dose-response relationship for lung cancer was obtained and analyzed according to the multiple NTCP-based LASSO model and DMH as input data in the NTCP model compared with DVH. There was a relationship between the irradiated volume (IV) 20, mass, the mean lung dose parameters, and radiation pneumonitis in the study patients. The current study results indicated that pulmonary function changes occurred 6 months after RT in the patients. Owing to the structure of lung, the current study indicated that DMH had important effect on the evaluated model.

■ Modulating Effects of Saffron and Melatonin Combined Regimens on Radiation-induced Cell Death and Clastogenic Effects Expressed as Micronuclei on Hela Cells

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Abstract:

Background: Ionizing radiation induces a wide variety of cellular damages including DNA damages leading to cell lethality. Different efforts were made during the recent years to countermeasure radiation insults on cells using natural and synthetic agents. However, there is no well-tolerated and well accepted agent for radioprotection. The current study aimed at evaluating the effects of saffron and melatonin, natural agents, on the radiation cell damage.

Materials and Methods: Hela cells obtained from the National Cell Bank of Iran (NCBI) were cultured using the standard methods. Cells were treated with either saffron or melatonin or in a combination form 2 hours before irradiation with 2 Gy gamma rays generated from a cobalt-60 source. Antioxidant activity of saffron and melatonin was assessed using the DPPH (2,2-diphenylpicrylhydrazyl) assay. Viability of cells was assessed using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay 48 and 72 hours after cell plating. Micronuclei assay was done by the standard method using the cytokinesis blocked micronuclei assay. At least 1000 binucleate cells were scored for the presence or absence of micronuclei.

Results: The DPPH assay showed a reasonable antioxidant activity at the dose range used in the current study. MTT assay showed reduced cell viability after the radiation of various doses of gamma ray (2-8 Gy) 48 and 72 hour after culturing. Treatment with saffron and melatonin led to increased viability of irradiated cells. Moreover, combination of both agents led to more significant effects on cell viability. Ionizing radiation induced a high frequency of micronucleus formation in binucleate Hela cells. Treatment of cells with saffron and melatonin alone or in combination led to a significant reduction in radiation-induced micronuclei formation.

Conclusion: Ionizing radiation induced cell lethality through clastogenic effects on DNA. Both saffron and melatonin were capable of maintenance of cell viability after irradiation and also both agents reduced radiation-induced micronuclei. The effects were more pronounced using a combination regimen of both

ABSTRACT

agents. Results of the current study indicated both saffron and melatonin could increase cell viability through reduction of clastogenic effects of ionizing radiation.

■ Early Colorectal Cancer Detection by the Fluorescence Spectroscopy of Blood

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Abstract

Background: The colorectal cancer (CRC) is the 3rd most common cancer in the world. Early cancer diagnosis is of much interest for researchers as it is highly preventable. Alteration of cancer-attributed blood fluorophores, as a cancer biomarker, and applying fluorescence spectroscopy (FS) to trace them accurately are also introduced in several literatures in which porphyrin is the most famous fluorophore. The current study aimed at detecting cancer at early stages by the FS of blood plasma.

Materials and methods: Plasma samples were obtained from 3 groups of healthy, benign dysplasia, and CRC cases. The samples were mixed with analytical grade acetone in a concentration of 1:1, centrifuged, and then, supernatants were collected. The FS was performed at the porphyrin excitation maxima (405 nm). The obtained spectrums were normalized. To detect the porphyrin more precisely, FS of plasma samples were performed at 450 nm. Then, the 405-nm and 450-nm wavelengths were subtracted to obtain the porphyrin peak.

Results: The detected spectrums had a prominent, wide peak in the range of 450 to 600 nm and an embedded little peak about 620 nm that was attributed to porphyrins.

Discussion and Conclusion: No significant differences were observed between the porphyrin peak of healthy and CRC cases in normalized unique porphyrin spectrums and plasma. It may be caused by unavoidable limitations affecting the porphyrin fluorescence including unequipped laboratory, conflicting biological disorders, and environmental interferers (lifestyle and habits). In the current study, a shift was observed in the prominent wide peak of CRC specimens. The criterion was not reported before and surprisingly could differentiate healthy and CRC samples with the sensitivity and specificity of 70% and 100%, respectively. The accuracy, positive predictive value (PPV), and negative predictive value (NPV) were more than 90%, 100%, and 88% respectively in the current study; hence, the accuracy of the method employed in the current study was more than that of carcinoembryonic antigen (CEA), the most commonly used colon cancer biomarker.

Keywords: Colorectal Cancer; Fluorescence Spectroscopy; Plasma Porphyrin; Early Cancer Detection

■ Application of Deformable Image Registration in Dose Integration of High-dose Rate Cervix Brachytherapy

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Abstract

Background: During the high-dose rate (HDR) cervix brachytherapy, dose received by the organ at risk (OAR) such as rectum and bladder cannot be calculated accurately because of interfraction variation of applicator position and organ deformation. The worst-case scenario from the International Commission on Radiation (ICRU) recommendation was to add maximum doses to the volume of 2 mL of every organ (D2cc) from every session. The D2cc approach may lead to overestimation of dose to these organs. Deformable image registration (DIR) can be used as a technique to register isodoses curves from different sessions and consequently lead to calculating the accumulated volumetric dose irradiated to the target as well as OAR accurately. In the current study, DIR was investigated in order to determine cumulative doses to the rectum and bladder from different HDR cervix brachytherapy sessions.

Materials and Methods: Thirty patients with locally advanced cervical cancer treated by external beam radiotherapy (EBRT) and 3 to 4 fractions of HDR brachytherapy (HDR-BT) were enrolled in the current study. Intensity-based B-spline algorithm was used as the primary DIR technique by the 3D slicer. In the dose integration stage, total doses of rectum and bladder from all brachytherapy sessions were integrated by the verified deformable image registration techniques.

Results: Results of the current study showed that the use of preprocessing can improve registration accuracy, especially for intensity-based algorithm. DIR encountered less mismatch error compared with that of rigid registration. Although the uncertainty on the accumulated dose by DIR was very small, duo to the high gradient dose in brachytherapy, a small error might remain a significant impact on dose distribution.

Conclusion: The current study showed that the intensity-based DIR techniques were more accurate than the feature-based techniques. It may be due to lack of user interaction. The intensity-based registration was sensitive to noise and required preprocessing at first. Finally, DIR can be used to increase the accuracy of dose irradiated to OAR tissue.

Keyword: Deformable Image Registration; Brachytherapy; Dose Accumulation

■ A Genetic Polymorphism in *CYP1B1* Gene as a Biomarker for Patients With Esophagus Squamous Cell Carcinoma: A 10-Year Mashhad, Iran, Cohort Study

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Abstract

Background : Esophageal cancer) EC (is the 8th most common cancer worldwide .In particular ,cytochrome P450 ,family 1 ,subfamily B) ,*CYP1B1*) polypeptide1 play an important role in nicotinamide adenine dinucleotide phosphate (NADPH)-dependent mono-oxygenation of a variety of substrates including steroids, fatty acids, xenobiotics, and metabolic pathways. In contrast, genetic variants in *CYP1B1* gene were found to be associated with the risk of several developing malignancies. Therefore, the present study investigated the impact of CYP1B1-rs1056836 on patients with esophagus squamous cell carcinoma (ESCC).

Method :A total of 317 subjects, with and without ESCC, were recruited. DNA was extracted and followed by genotyping via the real-time polymerase chain reaction (PCR)-based Taq Man. The Kaplan-Meier curves were utilized to assess overall and progression-free survival. To evaluate the relationship between patients' clinicopathological data, genotypic frequencies, disease prognosis, and survival, the Pearson chi-square and *t* tests were used. Logistic regression was utilized to assess the association between the risk of ESCC and genotypes.

Results : The genotypic frequency for GG ,GC ,and CC were 58.6%, 29.8% ,and 11.5% respectively in the healthy group and 51.8%, 36.14% ,and 12% respectively in the ESCC group .With respect to the recessive genetic inheritance model ,a significant association was found between the GG genotype and stage of ESCC .Also, there was no statistically significant relationship between this variation and risk of ESCC .Patients with GG genotype had a decreased risk for nodal metastasis in comparison with the ones with CC/CG genotype ,although this association was not statistically significant.

Conclusion : Findings of the current study indicated CYP1B1-rs1056836 as a potential biomarker for ESCC ,supporting further studies in larger population in different ethnic groups .Moreover ,further investigations are recommended to evaluate the association of emerging marker with dietary intake and lifestyle.

Keywords : Cytochrome p450 ;Esophagus Squamous Cell Carcinoma ;Dietary Intake ,Lifestyle

■ **Phytosomal Curcumin Inhibits Tumor Growth in Wnt-driven Colorectal Carcinoma**

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Abstract

Background: Colorectal-cancer (CRC) is the 3rd leading cause of death due to cancer, supporting the need for identification of novel anticancer drugs to improve the efficacy of current therapies. There is growing bodies of data showing the antitumor activity of curcumin, although its efficacy with respect to low absorption is associated with several limitations. The current study aimed at exploring the therapeutic potential of novel phytosomal curcumin as well as its application in combination with 5-flurouracil in a mouse model of colitis-associated colon cancer.

Methods: The anti-proliferative activity of phytosomal curcumin was assessed in 2- and 3-dimensional cell culture models. The expression levels were investigated by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) and Western-blotting techniques. The study evaluated the anti-inflammatory effect of this agent by pathological-evaluation and disease activity index (DAI). Moreover, antioxidant-activity was examined by malondialdehyde (MDA), total thiols (T-SH), superoxide dismutase (SOD), and catalase (CAT) activity parameters.

Results: Results of the current study showed that phytosomal curcumin and its combination with 5-FU inhibits cell growth and invasive behavior of CRC cells through the modulation of Wnt-pathway. Combination of this with 5-FU dramatically reduced the tumor number and tumor size in both distal and middle parts of colon followed by reduction in DAI. Also, curcumin suppressed the colonic inflammation induced by disease specific survival (DSS) and notably recovered the increased levels of MDA and decreased activity of CAT/thiol levels.

Conclusions: The study demonstrated the antitumor-activity of novel form of curcumin in CRC, supporting further investigations on the therapeutic potential of this approach in CRC.

Keywords: Colorectal Cancer; Phytosomal Curcumin; Anti-Tumor Effect; Colitis-associated Colorectal Cancer

■ **Evaluation of the Dose Delivered to Small Bowel in Patients With Rectal Cancer: A Look Inside Different Positioning of Patients**

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Abstract

Background: Delivering minimum radiation dose to the small bowel and femoral heads are of great importance in patients

with rectal cancer. The current study aimed at reviewing the effectiveness of different positions in radiation therapy in patients with rectal cancer.

Methods: Twenty patients with rectal cancer and the mean age of 53.2 years referring to Haft-Tir Radiotherapy Center (Tehran, Iran) were participated in the current study. Patients and their positions were divided into 2 groups: group A, 10 patients with 2 positions including prone with belly board (A_1) and without belly board (A_2); group B, 10 patients with 2 positions of supine (B_1) and prone with belly board (B_2). All patients were subjected to the computed tomography (CT) simulation with full bladder and treated with 15 MV photon beams. The 3-beam technique (2 opposed lateral and a posterior fields) were used to configure beams. Treatment planning techniques used for patients in groups A and subgroup B_2 comprised of 2 opposed lateral and a posterior fields and the box technique was used for patients in subgroup (B_1).

Results: Results show that small bowel dose in subgroup A_2 was significantly lower than that of A_1 (P value <0.05). Comparison of the results of B_1 and B_2 showed a significant difference in small bowel dose between the 2 groups. Also, in patients of subgroup B_1 with 4 fields, a significant reduction was observed in the dose delivered to femoral head in comparison with other subgroups.

Discussion: Results of the current study showed that prone position of patients with rectal cancer on belly board was more effective in reducing the dose delivered to the small bowel. Especially in patients with fatty and fallen belly, use of belly board could be very effective in reproducibility of patients positioning and reduction of the small bowel dose.

■ Blood Porphyrin Fluorescence Peaks and Their Diagnostic Values for the Early Colorectal Cancer Detection

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Abstract

Objectives: Porphyrins are the precursors of heme metabolism. Any metabolic disorder such as cancer can highly affect their levels. Since they are natural fluorophores, it is easy to trace them in blood. That is why the blood porphyrin fluorescence peak alteration is frequently considered as a promising cancer biomarker. The current study aimed at answering this question: Considering the clinical and laboratorial limitations, could porphyrin be a promising biomarker for CRC?

Materials and methods: Different fluorescence spectrums of both plasma and whole blood samples of the 2 groups of non-CRC (n=22) and CRC (n=10) were obtained. Based on previous reports and practical experiences, the optimum fluorescence spectrophotometry conditions were chosen for excitation and the porphyrin characteristic peak about 630 nm was used as a criterion for CRC detection. Moreover, for a better detection, an improving approach was applied as follows: the blood samples were excited at 450 nm and the emission spectra was used as a background filter in such an extent that porphyrin peaks were uncovered more distinctly. In addition, excitation-emission-matrix (EEM) was achieved.

Results: Despite a bunch of former reports showing the ability of porphyrin peaks to differentiate between CRCs and healthy subjects accurately, no prominent differences were observed in blood and plasma samples in the current study. Even distinct porphyrin peaks detected from total spectra by a novel trick could not differentiate the subjects. Nevertheless, a prominent peak about 500 nm was observed.

Discussion and Conclusion: Despite frequent reports on the promising early cancer diagnosis by porphyrin level in blood, the current results showed that it might not be reliable for CRC detection. It may be caused from several unavoidable limitations affecting the porphyrin fluorescence including unequipped laboratory (operator-based errors), conflicting disorders (other disorders affecting porphyrin level; e g, anemia) and environmental interferers (lifestyle and habits; e g, smoking). Therefore, the current study suggested the use of other peaks (i e, 500 nm) or EEM alternatively.

Keywords: Blood Porphyrin; Fluorescence Spectroscopy; Early Cancer Detection; Diagnostic Value; Colorectal Cancer

■ Assessment of Peripheral Organ at Risk Dose in IMRT versus VMAT in Prostate Cancer Treatment Planning Systems

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Abstract

Introduction: The accuracy of out-of-field dose due to the secondary cancer risk is clinically very important. The present study aimed at reviewing and comparing the peripheral dose between 2 modern techniques of intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) in prostate cancer.

Methods: Radiotherapy treatment planning systems are not commissioned for the out-of-field dose calculations, which affect the accuracy of dose beyond the borders of treatment fields. Now days using modern radiotherapy technique such as VMAT and IMRT because of many advantages are most common, particularly for patients with complex shape of planning target volumes such as prostate cancer; on the other hand, these techniques have some disadvantage including the increased time delivery and high number of monitor units (MU) in comparison with conformal radiotherapy. These higher number of MUs result in the increased peripheral dose, which generally is known as low-dose region. The component of out-of-field dose includes patient scatter, phantom scatter, and head leakage. Use of multi-leaf collimators in IMRT and VMAT can increase the leakage radiation contributions to out-of-filed dose. Based on many studies, patient scatter is the main dose

distributions near the filed edge, while leakage is more contributed at large distances from the filed edge. The increased peripheral dose distributions can potentially increase the risk of secondary cancers after IMRT. According to evidence, increase in collimator scatter and head leakage were estimated to increase (double) carcinogenic risk. Meanwhile many studies indicated the poor accuracy of out-of-filed dose in treatment planning systems. Prostate cancer is one of the most common cancers, and due to unwanted radiation from out-of-field organs such as rectum, bladder and head of femur, it may cause secondary cancer after radiotherapy.

Results: According to the results of many studies, increasing the distance from field edge increases the underestimation of dose calculation accuracy approximately 40% up to 10 cm; for example, in femoral head, TPS (tissue polypeptide-specific antigen) accuracy worsened to 20% for the 5-field IMRT, while 5% underestimation of Oncentra TPS were reported for near organs, bladder, and rectum. Generally, VMAT in comparison with IMRT, significantly reduced MU usage and treatment delivery time (P <0.05); it means that leakage of the out-of-field dose was smaller, while the scatter dose got enlarged 20% approximately.

Conclusion: Quiet understanding of peripheral dose resulting from VMAT and IMRT in prostate cancer is important in clinical settings. Physicians should estimate the organ at risk (OAR) dose and also risk to patients. The VMAT technique is more effective in the treatment of prostate cancer compared with IMRT due to providing lower peripheral doses for normal tissue complications. Actually many parameters affecting the peripheral dose in each TPSs and each technique even in each cancer was not specifically understood, in spite of many studies on the out-of-field dose.

Keywords: IMRT; VMAT; Peripheral Dose; Prostate Cancer

■ Clinicopathologic Characteristics of Basal and Non-basal Types Triple-negative Breast Cancers

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Abstract

Introduction: Breast cancer is a major health problem of females worldwide that has an increasing trend. According to genomic phenotype, there are 5 different types of breast cancer including triple-negatives with rather different treatment options and prognosis. It was supposed that the basal type triple-negative cancer especially has more aggressive manifestation and worse prognosis. In the current study, some disease variables were compared in this type of breast cancer.

Materials and methods: A total of 95 patients with triple-negative breast cancer according to surgical and pathologic results were included and the immunohistochemistry (IHC) analysis for some specific basal markers such as EGFR and CK5/6 were performed. Based on the obtained data, the study subjects were divided into basal and non-basal subtypes, and clinical and pathological variables were compared.

Results: According to the results of the current study, 82% of patients were basal and 18% non-basal. Comparison of these 2 groups showed a statistical significant difference about more lymph node involvement and higher histological grade in basal subgroup with p-values of 0.019 and 0.036, respectively. Other variables such as age, tumor size, perineural and lymphovascular involvements did not show any significant differences between the 2 subgroups.

Conclusion: Triple-negative breast cancer is a heterogeneous type of breast cancer comprised of basal and non-basal subtypes. Non-basal breast cancer has better trend in pathological variables such as lymph node involvement and histological grade. On the other hand, lack of relationship between the 2 subgroups in variables such as lymphovascular and perineural invasions, and tumor size in the current study might be due to the lack of data in the pathologic reporting system of some centers.

Keywords: Basal Type; Breast Cancer; Triple-negative

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■ Cytogenetic Bioindicators as Predictive Biomarkers for Low-dose Ionizing Radiation-related Cancer Risks

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ABSTRACT

Abstract

Ionizing radiation is considered as a known human carcinogen .Radiation apparently does not cause unique types of mutations ,but simply increases the mutations rate above their natural rate of occurrence .There is evidence indicating induction of cancer after low-dose exposures of diagnostic radiation in children and after in utero exposures .The growing use of ionizing radiation in medicine both for diagnostic and therapy purposes leads to the exposure of many individuals to low-level ionizing radiation occupationally or at general population level .Despite advancements in radiation protection and its implementation in clinical settings ,unfortunately the average yearly doses of patients due to medical exposure increased from 0.5 mGy in 1982 to 3 mGy in 2006 .At low doses ,radiation risks are primarily stochastic effects ,namely genetic effects and in particular ,somatic effects) cancer (rather than the deterministic effects characteristic of higher-dose exposure .Low doses of ionizing radiation received by radiation workers are not detectable by personal dosimeters such as film badges and pen dosimeters .On the other hand ,genetically a significant dose received by general population may contribute to the increase in genetic defects and probably cancer in general population .Therefore ,there is a need for cancer risk biomarkers for such situations .Ionizing radiation is a potent inducer of both chromatid and chromosome type aberrations due to initial unrepaired or misrepaired DNA damages .Previous studies suggested that the frequency of chromosomal aberrations)CAs (predicts cancer risk and confirm that a high level of CAs is associated with an increased risk of cancer and indicated that this association does not depend on the time between CA analysis and cancer detection .The study of CAs can be done simply on peripheral blood lymphocytes to predict and estimate cancer risk in exposed individuals .However ,there should be enough support from policy makers to use CA analysis as a tool in screening programs and prevention policies in occupational and environmental health.

Keywords: Low-dose Ionizing Radiation; Cancer Risk; Chromosomal Aberrations; Cancer Biomarkers

■ Correlation of Radiation-induced γH2AX and Gene Expression in Sporadic Ductal Carcinoma of Breast Tumor Tissue With Cytogenetic Findings in Lymphocytes

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Abstract

Radiosensitivity of the patients with breast cancer is shown previously and adverse effects of radiotherapy in such patients often lead to clinical complications; however, intrinsic radiosensitivity of tumor tissue and peripheral blood lymphocytes, mainly used to assess radiosensitivity, is a question. The current study aimed at investigating different individual responses to gamma-rays with different expression levels of ATM and HER-2 and unrepaired DNA double-strand breaks (DSB) observed as γH2AX at tumor, normal adjacent tissue level of patients with breast cancer, and the frequency of chromatid type aberrations in G2-irradiated lymphocytes.

Sixty patients were enrolled in the current study. The ductal carcinoma of breast, normal adjacent and normal tissue samples, obtained following surgery were exposed to a 4-Gy gamma irradiation in a complete culture medium. After 24 hours incubation in modified RPMI 1640 medium at 37°C in the atmosphere with 5% CO_2, the frequency of residual-induced DSB was assessed using γH2AX assay and compared with those of the pair normal adjacent and control breast tissue samples. The samples from similar tissue were used for RNA extraction and expression assay with real-time polymerase chain reaction (PCR) to quantify ATM expression. HER2 was assessed using immunohiscochemical and PRINS techniques. Chromatid aberrations were scored in lymphocytes exposed to 1 Gy gamma-rays using the standard G2-assay technique.

The current study results showed that the frequency of DSB dramatically increased in both tumor and normal irradiated tissue samples, compared to the sham non-irradiated controls. Tumors with HER-2 overexpression showed significantly lower residual DSB frequencies after 24 hours post-irradiation incubation time, whereas this frequency dramatically increased in ATM underexpressed tissue. Frequency of patients with elevated chromosomal aberrations in lymphocytes clearly correlated with the frequency of γH2AX.

The obtained results indicated that different tissue samples may have different radiosensitivity and ATM underexpression and HER-2 overexpression may lead to higher and lower sensitivity to ionizing radiation, respectively. This may be due to the role of ATM in DSB repair and HER2 in epidermal growth factor receptor (EGFR) downstream signaling pathway that with the use of cell survival mechanisms ends in resistance against radiation effects using non-homologous end joining (NHEJ) pathway and activation of PI3K/ACT that leads to DSB repair.

■ The Effect of Spiritual Counseling on the Health of Females With Cancer

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Abstract

Background and objectives: Spirituality is one of the important dimensions of human health. Considering the painful nature of cancer and the spiritual crisis in patients, the current study aimed at investigating the effect of spiritual counseling on the spiritual well-being of females with cancer.

Materials and Methods: The current study clinical trial was performed on 42 females with cancer referred to Shahid Beheshti Medical Center in Hamedan city, Iran. The subjects were

randomly selected and with random allocation method assigned into the intervention (n=21) and control (n=21) groups. Data were collected by Paloutzian and Ellison spirituality health questionnaire. The intervention included 8 sessions of 45 to 60 minutes spiritual counseling sessions for the intervention group. Spiritual health was measured in 2 steps, before and after the intervention, and analyzed with SPSS software version 20 using statistical methods.

Results: In the current study, the means of spiritual well-being were 96.86 ± 12.71 and 111.05 ± 5.15 before and after the intervention, respectively. The t test results indicated significant increase of the spiritual health of the patients in the intervention group (P-value $\square 0.05$).

Conclusion: The results of the current study showed that spiritual counseling played an effective role in the process of recovery and admission of the disease and increased the level of spiritual health in the studied patients; therefore, it is recommended that nurses use the spiritual counseling method to treat such patients.

Keywords: Spiritual Health; Cancer; Spiritual Counseling

■ Seeking for Peace; a Basic Requirement in Patients With Cancer

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Abstract

Background and Objectives: Spirituality is considered as a source of compatibility in patients with cancer. The increasing incidence of the disease and the belief that peace is more important than ever during illness shows need to relaxation in patients.

The current study aimed at determining the Search for peace in the patients with cancer in Iran.

Method: The current study was a qualitative content analysis. Participants in the study included 18 patients with cancer admitted from April to September 2013 to Cancer Institute of Imam Khomeini in Tehran. The Purposive sampling method was used and continued until data saturation. The interview was used to collect data. The conventional content analysis was performed and the relevant themes were extracted.

Discussion and result: A total of 671 codes were obtained from the original codes and data themes were extracted in 3 realms of need for seeking inner peace, begging forgiveness and hopefulness, and subcategories as the need to be alone, patient's actions in face of the disease, being patient, the effects of the disease , forgiving sins, forgiving others, hopeful for healing, hopeful to God's assistance, and not merely healing.

Keywords: Peace; Spiritual Needs; Cancer; Iran; Nurse; Care

■ Cancer Stigma and Responses to Diagnosis

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Abstract

Introduction: Detection of cancers is associated with several reactions. These reactions are aggravated by the presence of stigma, negative beliefs, and stereotypes about it. The presence of this stigma causes other effects and consequences such as the lack of referral for the diagnosis or follow-up of treatment, and the impairment of the individual, family and social life of people with cancer. The current study aimed at investigating the relationship between the response to the diagnosis of disease and cancer stigma.

Method The current qualitative study was conducted with the participation of patients with cancer ,their families ,and the treatment team. The purposive sampling method was used and data were collected through semi-structured interviews .The data were analyzed and managed using MAXQDA version 10 software by conventional content analysis method.

Results: The analysis of the data collected from the interviews showed that the diagnosis of cancer was as a *feeling of being lost in unknown darkness*. Subcategories included *lack of psychological readiness, psycho spiritual disturbance, denial, severe and irrational reactions, and confusion.*

Conclusion: Cancer stigma clearly affects the responses of individuals to diagnosis. Considering the presence of stereotypes and their impact on people's responses to the diagnosis of the disease is important and also is another aspect of controlling the disease and quality of life of affected people and their families. Designing and implementing effective interventions to reduce stigma helps to reduce fear of cancer and improve the quality of life of individuals with cancer.

Keywords: Cancer; Stigma; Psychological Responses; Iran

■ The Nurses' Attention to Religion in Caring With Patients With Cancer

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Abstract

Background and Objectives: It is very important to understand the needs and problems of patients, especially after exposure to cancer diagnosis; due to the increasing number of patients with cancer, the threatening nature of cancers and the problems they cause for patients and families. Today, many physicians know religion and beliefs as an important source of physical health and well-being, and they consider spiritual issues essential in the process of treatment. Hence, the religions help the patients to adapt to the diagnosis of cancer. Understanding the needs of patients with cancer and their interests helps the professional staff, especially nurses, to provide appropriate counseling services for patients and families.

Method: The current review study on the role of religion in caring for a cancer patient, reviewed different articles in reliable local and foreign electronic websites along with the library resources, and scrutinized different research findings. Then, through gathering the required data, analyzed the data on nurses' attention to religion in caring the patients with cancer.

Discussion and result: Religion is considered as an important source of adaptation for the patients with cancer. In the patients with cancer, religion is beneficial to maintain self-esteem, provide the sense of meaning and purpose, create emotional relaxation, and enhance hope. There is increasing evidence that spiritual and religious practices, beliefs, and attitudes of the patients have a great impact on their health outcomes. Patients are relaxed with this need, because they believe that the presence of a strong force and secure shelter is the first factor to achieve a deep relaxation. In religious societies, such as Iran, this is more than other societies due to the greater belief in God's presence in everyday life of the people. In such a society, in the time of despair and self-deprivation of the patients, paying attention to the Lord's support revives the patients` hope.. Research shows that most patients turn to religious approaches to improve their mental and mental health in order to cope with stresses of the disease and execution of death. Older patients are more likely to pray and refer to the Bible than others. Therefore, the religious source for patients with cancer is an important adaptation resource used during the disease process. This source is compatible with the various effects of diagnosis and treatment, especially chemotherapy. Individuals' satisfaction from their lives, better adaptation, pain relief, and reduced anxiety are related to death. Therefore, support from a religious source and having relationship with a higher power can be beneficial to improve quality of life and interpersonal support, reduce the severity of symptoms, and lead to appropriate medical results.

Keywords: Religions; Cancer; Iran; Nurse; Care

■ The Age-appropriate Supportive Care Needs of Adolescents With Cancer :A Qualitative Study

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Abstract

Purpose: The current study aimed at assessing the viewpoints, experiences, and preferences of adolescents with cancer, their parents and healthcare providers concerning the age-appropriate supportive care needs of adolescents with cancer.

Methods: It was a qualitative, descriptive-exploratory study on 33 participants (adolescents diagnosed with cancer aged 15to 20 years, their parents, oncologists, and nurses). In-depth semi-structured interviews were conducted and data were analyzed using open and axial coding of constant comparative analysis.

Results: Data analysis yielded 4 main themes; the requirement for a care model tailored to the needs of adolescents with cancer, the facilities preferred by adolescents with cancer, the need to categorize patients based on age and severity of their condition, and the need to create a space similar to home in hospitals.

Conclusion: The results emphasized on the necessity of development and implementation age-appropriate programs in healthcare centers and institutions, the supply of appropriate equipment and facilities for these centers, and the adoption of multi-disciplinary healthcare models for adolescents with cancer to answer their specific medical, physical, and support needs, which enhance the life quality of adolescents with cancer.

Keywords: Adolescents With Cancer; Facility Needs; Parents; Health Care Providers; Qualitative Research

■ Cancer Reality With Astringent Taste From the Perspective of Patients, Families ,and Caregivers :A Qualitative, Content Analysis

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Abstract

Introduction: In the present century, one of the biggest challenges that health systems around the world are facing is the spread of chronic diseases; diseases that are the result of modern lifestyles, increased exposure to risk factors, and the growth and development of lifesaving treatments and care. Cancer is a chronic disease and one of the major health problems worldwide. More than 25 million people in the world are currently living with cancer. After cardiovascular diseases and accidents, cancer is the 3rd leading cause of death in Iran. The incidence of cancer in Iran is approximately 84,829 persons, and the annual mortality rate is reported as 53,350 individuals. Several crises threaten the patient since the diagnosis of the disease, and they include feelings such as fear, anxiety, depression, and frustration. Therefore, chronic illnesses or severe illnesses cause shock, distress, distrust, fear, and depression in the patient; care providers should be prepared to respond to the patients` needs.

ABSTRACT

Learning to live with chronic disease is a process in which health care providers can play a role in assisting the patient to adapt to it. Therefore, understanding the patient, the family, and the caregivers perspectives can help identify their problems and care needs. The current study aimed at explaining the patients, the families, and the care providers` perception of cancer.

Method: The current qualitative study was performed from 2016 to 2017. Data were collected using semi-structured interviews with 16 participants in the study including patients with cancer, their families, physicians and nurses. The study was conducted in the oncology wards of the hospitals affiliated to Shahid Beheshti University of Medical Sciences (Imam Hossein and Shohadaye Tajrish hospitals) as well as Firoozgar Hospital affiliated to Iran University of Medical Sciences and the Alla Cancer Prevention and Control Center. Lundman and Graneheim methods were used to analyze the data. MAXQDA version 10 was used for data analysis.

Results: The main themes emerging from the data were astringent taste of reality including 2 categories of uninvited guests and oncology atmosphere; the uninvited guests category consisted of 4 sub-categories; an unpleasant appearance, an unexpected occurrence, hope, and confrontation with death. Oncology atmosphere comprises 2 subcategories as comprehensive empathy and heavy space. The findings of the current study, based on participants' experiences, describe the cancer as an astringent reality, which reflects the experiences of patients with cancer and its good and bad aspects. The negative and sometimes misconceptions associated with the disease have made it an uninvited guest. Although cancer may be associated with patient's death, there are glimpses of hope in patient. Just as in the oncology ward that in addition to the unpleasant atmosphere and unfortunate events opens a window to intimacy and affection for the residents. This is a narrative of the taste of cancer.

Conclusion: The findings of the current study can help the care team members recognize the needs and concerns of patients for comprehensive and holistic care.

■ Breast Cancer: A Phenomenological Study

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Abstract

Introduction: The breast cancer is the most common cancer in females and the second leading cause of death in the age range of 35-35 years. The healthcare team needs a comprehensive understanding of the experiences of patients and their families. The current study aimed at describing the structure and nature of the experiences of patients with breast cancer.

Methodology: In the current qualitative study with a phenomenological approach, sampling was started after obtaining the necessary permissions and referring to the oncology clinics affiliated to Arak University of Medical Sciences, Arak, Iran. The target-based sampling method was continued until the data sat-

uration. Twenty-two participants (patients, families, and healthcare team) participated in the study. Data were collected using in-depth interviewing and were analyzed by the Parse method. It was tried to analyze qualitative data based on the valid criteria.

Results: The findings of the current study were summarized into 4 core concepts: delay in diagnosis and treatment, treatment rejection, drowning in suffering (emotional reactions to the disease, facing the outcomes of treatment, exposure to treatment system, ineffective care and disturbance in daily life of the family), and moving toward normal life.

Conclusion: Knowledge of treatment team from the experiences of females with breast cancer helps them to play a better role in their treatment. It seems essential to shift from terminal treatment to early diagnosis. Also, it is emphasized to use a source to support patients.

Keywords: Breast Cancer; Mastectomy; Chemotherapy; Phenomenological Study

■ The Effect of Self-care Education on General Health and Life Expectancy in Patients With Cancer: A Review Study

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Abstract

Background and Objective: Hopeful spirit is one of the most important and essential elements in patients with cancer, which has a great impact on the adaptation of patients with living conditions, especially during pain and deprivation. Self-care is defined as a strategy to adapt to events and tensions in life, which increases the aging process, involves special activities by which the symptoms of the disease are reduced, and maintains and upgrades the health of patients. Today, the discussion about patient education is about self-care and should provide conditions that patients can take care of themselves.

Methods: To determine the effect of self-care education on general health and life expectancy in patients with cancer, the current study searched in PubMed and Science Direct databases as well as SID and reviewed relevant articles published from 2006 to 2016. Full text articles meeting the inclusion criteria were retrieved and reviewed.

Findings: Of the 5837 titles identified, 47 articles were included in the current review. The current study evaluated the efficacy of patient self-management educational programs for chronic diseases and critically reviewed their methodology. Results of the review of the studies indicated that self-care education had a positive effect on self-care behaviors and life expectancy in patients with cancer.

Conclusion: The results of the current study showed that quality-of-life in patients with cancer can be improved by participating in self-care education programs. Therefore, it is suggested that self-care education should be added to routine nursing care for such patients. Self-management education for chronic illness may soon become an integral part of high quality primary care.

Keywords: Education; Self-care; General Health; Life Expectancy; Cancer

ABSTRACT

■ Impact of Implementation and Education of Physical Activity and Sport Program on Survivors of Breast Cancer :A Systematic Review

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Abstract

Background: Breast cancer is one of the most common cancers among females .It is a chronic disease due to its unfavorable survival .Sports and physical activity training programs can change sedentary life style and survival rate and enhance active participation in their own health care .The current study aimed at recording and demonstrating integrated sports and physical activity educational programs for breast cancer survivors.

Methode: The Pub Med, ProQuest, Web of Knowledge, Embase, and Cochrane Library databases were reviewed with the keywords: sport program, physical activity program, survivor, and breast cancer.

Results: In 11 sports and physical activity training programs, the positive effects of the exercise program, exercise and physical activity included quality-of-life (QoL), anxiety, fatigue, depression, bone density, change in lifestyle with low mobility, function and heart parameters, oxygen consumption, physical activity, speed of motion, body mass index (BMI), waist circumference (WC), body fat, mental status, and increased physical activity in leisure time. In the 2 studies, the performance of exercise programs did not improve pelvic bone density. Also, in 1 study, no effect on BMI was reported.

Conclusions: Physical activity and sports programs varied from 2 to 24 sessions and were conducted by telephone, counseling, or in person, either on the web or in the presence of multimedia. Sport activities from moderate to severe or both including aerobic or resistance exercises or a combination of them were used in the current study. All programs were effective on a variety of physical and mental aspects, except one.

Implications for Breast Cancer Survivors: The design and implementation of physical activity and sport education programs can improve the QoL and reduce the complication of treatment of breast cancer survivors. Cancer nurses can design and implement these programs to enhance the QoL and preparation for a happy and high-quality life.

Keywords: Educational Program; Physical Activity; Exercise; Survivors; Breast Cancer

■ Investigation of the Effective Factors on Job Burnout on Sayedoshohada Hospital Nurses

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Abstract:

Background: Nurses are vulnerable to burnout. The current study aimed at investigating the effective factors on burnout in Sayedoshohada Hospital, Tehran, Iran in 2012.

Methods: The current correlational study was conducted on100 nurses selected by random sampling method. Data were collected by a questionnaire. SPSS version 19 was used for data analysis. Descriptive statistics was employed to describe the characteristics of demographic variables. Coefficient correlation and stepwise regression analysis were used in the inferential statistics.

Results: LMX, psychological empowerment, organizational commitment, and perceived organizational support had inverse relationship with burnout. But, family conflicts had direct relationship.

Conclusion: Results of the current study demonstrated the importance of organizational factors. The main suggestion of the current study was to hold educational workshops about burnout and moral distress.

Keywords: Burnout; Moral Distress; Nurses

■ Assessment of Factors Impacting the Quality-of-Life in Patients With Lung Cancer: A Systematic Literature Review

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Abstract:

Introduction: Lung cancer is the most common type of cancer and cause of death in the world. Considering complications and signs of lung cancer, assessment of the quality-of-life (QoL) of such patients is an essential part of cancer management.

Methods: The current comprehensive search included a combination of the keywords QoL, patients, cancer, and lung. Data were collected from the PubMed and Scopus databases and Science Direct and Ovid sites from 2010 to 2016.

Results: The results of the study on literature showed that the current survival rate of patients with lung cancer increased with the development of modern science to treat patients with lung cancer, but this increase in survival is often not associated with good QoL in the patients, and sometimes they encounter many problems. Many factors such as the symptoms of illness and sleep problems, diseases associated with pulmonary cancer, and even treatments for those patients with chemotherapeutic and surgical complications reduce the QoL in such patients. Also, daily habits such as

doing some exercises decrease QoL and increase smoking. Psychological factors also affect the QoL in such patients; therefore, social support is an important factor in improving QoL in such patients.

Conclusion: The findings of the current study revealed that there were significant factors affecting the QoL of patients with pulmonary cancer; therefore, the seemingly simple and non-essential factors had a significant effect on QoL of such patients. QoL and survival of patients with lung cancer are 2 dependent factors, which increase QoL of the patients, life expectancy also increases. Therefore, it is recommended to conduct a study in order to investigate these factors in Iranian patients, educate medical staff and families of the patients, and most importantly, educate the patient himself to increase self-efficacy and have a good life is a continuation of the disease.

Keywords: Quality-of-Life; Patients; Cancer; Lung

■ A Survey on the Impact of Bad News Disclosure Using Truth-telling Protocol on the Level of Stress, Anxiety, and Depression in Patients With Cancer

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Abstract:

Introduction: The employment of guidelines and protocols in disclosing the bad news of cancer diagnosis has a long history in Western countries, but in many non-Western countries, especially in the Middle East, there is still no guideline on this complex responsibility. In the current study, which was part of a larger mixed-method study, a protocol based on Iranian culture was developed for truth-telling to patients with cancer and then, attempts were made to implement this protocol in a quasi-experimental study with 2 intervention and control groups; and at the end, its effect on psychological factors of patients was evaluated.

Method: The study included 60 patients divided into 2 groups of intervention and control (n=30 in each group). In the intervention group, patients were informed about their cancer diagnosis using the developed protocol and through the members of the truth-telling team. In the control group, the cancer diagnosis was disclosed to the patients and their family members in the usual manner without using the protocol. Then, in 2 different intervals; i e, 3 and 8 weeks after the truth-telling, researchers assessed the stress, anxiety, and depression in patients using the DASS-21 questionnaire.

Results: The results of the current study showed no significant difference between the intervention and control groups concerning anxiety and depression variables 3 weeks after the truth-telling; but 8 weeks after the truth-telling session, all variables including stress, anxiety and depression had a significant difference between the intervention and control groups (P<0.05).

Conclusion: Despite the fact that 3 weeks after the truth-telling session, the patients in the intervention and control groups were not different in terms of the level of anxiety and depression, the level of stress in the intervention group was significantly more than that of the control group due to more information about the disease and treatment; however,8 weeks after the truth-telling session, all of the psychological parameters in the intervention group significantly improved compared to those of the control group. This finding can be attributed to better and faster adaptation of patients with their disease disclosure in the intervention group compared with the control group, and it can be considered as a consequence of effective implementation of truth-telling using the protocol developed in the present study.

■ Exploring Oncology Nurses Perception of Empathy Outcomes

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Abstract

Background: Review of literature showed that empathy with patients during caring can bring about different feelings in oncology nurses and patients. These feelings can be influenced by cultural factors. The current study aimed at exploring Iranian oncology nurses' perception of empathy outcomes.

Materials and method: The current qualitative study included 15 oncology nurses selected by the purposive sampling. A semi-structured face-to-face interview was conducted with each of the participants. After data collection, all interviews were transcribed and reviewed, and then, primary codes, sub-categories, and categories were extracted. The conventional content analysis method was employed to analyze the data.

Results: In the current study, the outcomes of empathy from the perspective of Iranian oncology nurses were extracted with 2 main categories including positive effects (benefit for the patients, benefit for the nurses) and negative effects (nurses' physical and psychological vulnerability).

Conclusions: Empathy is important for the patients with cancer. Therefore, it is necessary that policy makers and managers establish rules and regulations to reduce the negative outcomes in oncology nurses. Training the oncology nurses in empathic communication with patients may be beneficial and may also be cost-effective.

Keywords: Empathy; Outcome; Oncology Nursing; Qualitative Study

■ Perceptions of Oncology Nurses Regarding Barriers to Empathy-based Care

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Abstract

Background: As patients with cancer experience psychological distress, empathic care is necessary to reduce anxiety and increase hope. In addition, this type of care can positively affect their psychological adjustment. However, nurses devote little time to communication with patients In Iran.

Purpose: The current study aimed at exploring the perceptions of oncology nurses regarding barriers to empathy-based care.

Methods: The study applied a descriptive qualitative method; 18 oncology nurses were selected by the purposive sampling method. Data were collected through in-depth interviews and qualitative content analysis was used for data analysis with an inductive approach.

Results: Three main categories emerged from the data analysis: 1)barriers related to nurses included lack of a compassionate mind, lack of interest in oncology nursing and self-criticism, and psychological distress of nurses; 2)barriers related to health care system consisted of job strain of nurses, task-centeredness rather than patient-centeredness, lack of formal training, lack of support from manager, and nurse -patient gender imbalance; and 3) barriers related to cancer care comprised difficulty of maintaining empathy with cancer patients and sense of futility of care for patients with cancer.

Discussion: Listening to oncology nurses provided insight into empathy-based care barriers and the challenges they encountered while caring for cancer patients. Understanding these barriers is the first step to overcome obstacles and create an open and caring environment to provide an empathic care culture. Health care system should change organizational culture of caring for patients with cancer from task-centered to patient-centered. Compassion and empathy should be considered as values in patient care.

■ True Change or Response Shift on Measuring Quality-of-Life in Patients With Cancer

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Abstract

Introduction: In clinical studies, one of the main reasons to measure quality-of-life (QoL) changes over time is to evaluate the amount of the reported changes that are real and reflect errors. Evidence shows that patients with chronic diseases change their internal standards, values, and conceptualization of a target construct as their disease progress. This phenomenon reflects the response shift Thus ,response shift refers to a change in the definition of QoL over time .Recently ,there has been an increase in the number of studies ,which estimates response shift in individulas with chronic and life-threatening conditions .The completion of a systematic review in this area would improve our understanding of response shift's effect on the evaluation of QoL in cancer patients.Therefore ,this study was aimed to systematically compile and evaluate the existing evidence about response shift variation in QoL studies with cancer patients.

Material and Methods: In the current systematic review, 2 independent reviewers conducted a systematic search in the electronic databases including PubMed, Web of Science, Embase, and PsycINFO by search terms. All databases were searched without time limitation up to October 2017. The magnitude of response shift was examined through reported measures.

Results: A total of 45 studies was identified through the databases. Duplicate and irrelevant studies were removed by evaluating the titles and abstracts. Characteristics of the studies were determined. They used different scales and questionnaires to conduct QoL studies. They were heterogeneous in terms of cancer groups. Three main approaches were used to explore the effect of response shift. A majority of the studies applied the then-test method, which is also known as the retrospective pretest-posttest design.

Conclusion: Evaluation of QoL over time with self-reported questionnaires may be affected by the response shift. This effect can mask the real effects of specific events such as special care or treatment over time in the research outcomes. The current review emphasized the need for report and more sensitive method to find the clinical impact of response shift in QoL outcomes. Patient's adaptation to the disease can then be influenced by this effect; and adversely affect clinical decision making of health care team members.

■ Evaluating Effective Factors Related to Safety Precautions in Working With Chemotherapy Medications Among Nursing Staff of Chemotherapy Wards Affiliated to Mashhad University of Medical Sciences, Mashhad, Iran

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Abstract

Introduction: One of the therapeutic options to treat cancer or ameliorating its symptoms is chemotherapy. Owing to close contact with carcinogen chemicals in this type of treatment, standard principles and precautions should be considered as the basic requirement and necessity for staff working in this field as well as for the patients. The current study aimed at evaluating the level of safety precautions consideration in working with chemotherapy medications, the reasons not to follow them by nurses working in chemotherapy ward, and the existing problems in the safety conditions of professional environment.

Materials and methods: The current descriptive analytical study was performed on 36 nurses working in chemotherapy wards of hospitals affiliated to Mashhad University of Medical Sciences, Mashhad, Iran. Data gathering tool was a standardized questionnaire evaluating 6 domains: general demographic information, attitude toward self-efficacy, existence of professional predicaments, the level of perceiving dangers in chemo-

therapy medications, and the level of safety in professional environment and functional domain. Data were analyzed with SPSS version19, using descriptive statistical methods such as mean ± standard deviation, and analytical statistical method of the Pearson correlational coefficient.

Results: A total of 27 females and 9 males with the average professional experience of 8.12 ± 5.9 years were included in the study. The average work shifts in a week was 48 ± 6.12 hours. Shortage of time and lack of enough training were the main predicaments to meet the standard safety precautions in chemotherapy wards. According to the level of perception of dangers in work environment, it was found that all staff was concerned about the negative impact of chemotherapy drugs on their general health and 91% of subjects believed that these medications were harmful; 55% believed that the protective equipment in chemotherapy wards were inadequate. The Spearman correlational coefficient estimation demonstrated a significant linear correlation between using personal protective equipment and adequate training about working with chemotherapy drugs ($r= 0.391$, $P=0.019$)

Conclusion: Safety of work environment and adequacy of the number of staff per patient were the very effective factors considering safety precautions by staff in working with chemotherapy drugs. Therefore, adequate protective equipment should be provided in work environment. Moreover, insecure methods of working with these drugs should be modified and the adequate number of staff per patient should be hired in chemotherapy wards.

Keywords: Chemotherapy; Nurses; Safety Precautions

■ Empowerment Aspects of Families With Children Affected by Leukemia in Iran: An Exploratory, Descriptive Study

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Abstract

Introduction: Childhood cancer is a familial disease that affects the child, as well as all family members and even close relatives, associates and friends, and imposes a high burden of care on the family, and affects different aspects of family life. Basically, taking care of a child affected by leukemia is family-centered, and therefore, recognizing family needs and empowering them can play a significant role in taking care of the child. Therefore, the current study aimed at identifying different aspects of empowerment required to design a family empowerment intervention program.

Methods: Forty members of families with children affected by leukemia (18 mothers, 11 fathers, 11 sisters or brothers, and 4 patients) and 16 members of the treatment team (oncologist, internist, clinical psychologist, hospital managers, nurses, and cleric) were selected by the purposive sampling method. Data were collected through in-depth interviews and analyzed using a qualitative content analysis.

Results: Data analysis revealed the following 5 categories: management of physical, psychological, and social complications; effective

exposure to disease; management of social interactions; spiritual empowerment; comprehensive support for family empowerment.

Conclusion: Taking care of children with leukemia is a family-centered process and success is in the correct implementation of the program and the provision of proper care that depends on focusing on family as a unit and satisfying the needs of all family members. The focus of the treatment system should be changed from patient-centered to family-centered, meaningfully and comprehensively.

■ The Family Experience of Relationships and Interactions in Children With Leukemia: A Exploratory, Descriptive Study

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Abstract

Introduction: Childhood cancer is a familial disease that affects many aspects of family as a unit. One of the most important familial aspects significantly influenced by a familial history in childhood is individual and family relationships and interactions, Social, and family functioning. Family interaction and communication in family-based care is a critical and important factor. Therefore, the current descriptive, qualitative study aimed at exploring the perceptions of families of children with leukemia as well as the treatment team members in interactions and relationships of individual, family, social and family functioning.

Methods: A total of 40 members of families with the children affected by leukemia (18 mothers, 11 fathers, 11 siblings, and 4 patients) and 16 members of the treatment team (3 oncology specialist, 1 specialist, 1 person clinical psychologist, 2 hospital managers, 2 staff, 8 nurses, 1 cleric, and 1 hospital expert) were selected by the purposive sampling method. Data were collected through in-depth interviews and analyzed using a qualitative content analysis.

Results: Data analysis revealed the following main category: family empowerment in the management of interactions (intrapersonal, intrafamilial, and social) and 4 sub-categories including adoption and adaptation of the family by changing role models, revision and modification of family relations, improving and expanding social interactions in family, and the necessity of expanding and improving the family function.

Conclusion: Taking care of children with leukemia is a family-centered process and the prerequisite success for correct implementation of the program and the provision of proper care depends on the family's full attention as a unit and satisfies the needs of all family members. Therefore, the care of the child with leukemia is a family-centered process. Therefore, the focus of the treatment system should be changed from a patient-centric to a family-centered completely and comprehensively.

ABSTRACT

■ Body Image of Females With Breast Cancer After Mastectomy: A Review Literature

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Abstract

Introduction: Breast cancer is the most common cancer in females, which endangers individual aspects of mental health, quality-of-life (QoL), mental image, and sexual function. From the psychological aspect, breast cancer is the most effective cancer in females that includes 33% of all types of cancer in females. Breast removal through surgery is considered as destruction of part of the body, which is a symbol of gender, femininity, and maternal dimensions. Due to the importance of breast for the development of a female sexual identity, the response to the disease can include fear, anxiety, and depression. The consequences of treatment greatly affect their lives in the later stages, especially in relation to the problems caused by the person's mental image of the body and sexual function, which is an important part of QoL of the survivors of breast cancer. Body image plays an important role in the psychological function of patients with breast cancer.

Method: The current review study searched the keywords body image, breast cancer, and mastectomy in the Irandoc, PubMed, SID, Iranmdex, Magiran, and Science Direct databases.

Findings: A total of 150 articles were extracted from 2012 to the end of June 2017, of which a total of 40 articles were regularly used; 4 themes were regenerated from the study:

1. Provide psychological counseling to these individuals and their families, 2. Provide medical counseling before and after treatment, 3. Teach the patients to raise awareness, 4. Help the patients to cope with illness.

Conclusion: According to the results of the evaluated studies the mental image of the body decreased in females undergoing mastectomy surgery , which affects their job states, relationships with friends, and life expectancy.

■ Priorities of Care Infrastructures in Interprofessional Supportive Care of Patients With Cancer Undergoing Chemotherapy in Iran; the Oncologists' Perceptions

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Abstract

Introduction: Patients with cancer undergoing chemotherapy have needs that are not met and oncologists play the major role in their supportive treatment. The current study aimed at describing Iranian oncologists' perceptions in terms of priorities of care infrastructures in interprofessional supportive care of the patients with cancer undergoing chemotherapy.

Method: The current study was conducted using descriptive, exploratory, qualitative approach; the purposive sampling method was used for medical oncologists with the mean age of 47.5 years and mean work experience of 15.8 years from July to October 2016. Data saturation was achieved with 15 participants. Interviews were semi-structured and the Graneheim and Lundman qualitative content analysis approach and MAXQDA software were used to analyze the data.

Results: Two main categories were obtained from data analysis: 1. Continued comprehensive support in disease continuum from diagnosis to rehabilitation (education and consultation, social and treatment support for patient, the consideration of family support, addressing cultural condition, psychological support, and financial support); 2. Prerequisites in the preparation of the care system (the need to create interprofessional teams, development and improvement of health care settings to provide services, and empowering the health care team to provide quality care).

Conclusion: Comprehensive care for such patients and integration of these supports are essential in routine care. Major needs that should be addressed more seriously in the Iranian care system include the need for continued comprehensive support in disease continuum from diagnosis to rehabilitation and prerequisites in the preparation of the care system.

Keywords: Chemotherapy; Cancer Patients; Oncologists; Supportive Care

■ Do-Not-Resuscitate Order: The Experiences of Iranian Cardiopulmonary Resuscitation Team Members

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Abstract

Background: One dilemma in the end of life care is making deci-

sions to conduct cardiopulmonary resuscitation. This dilemma is perceived in different manners due to the influence of culture, religion, and race. The current study aimed at understanding the experiences of cardiopulmonary resuscitation team members about the do-not-resuscitate order.

Methods: The current qualitative study was conducted in teaching hospitals in an urban area of Iran from 2015 to 2016. Participants consisted of 24 nurses and physicians as the cardiopulmonary resuscitation team members selected by the purposive sampling method. Individual face-to-face semi-structured interviews were held to gather data. The collected data were analyzed using a conventional content analysis method.

Findings: The data analysis led to the development of 3 categories and 8 subcategories as follow: the determinants of the do not resuscitate order' with the subcategories of the chances of the cardiopulmonary resuscitation success, death as a cause for comfort, and physicians' individual differences; the challenges of the do not resuscitate order with the subcategories of legal challenges, ethical challenges and operational challenges; the consequences of the do not resuscitate order with the subcategories of reducing the motivation for the cardiopulmonary resuscitation and changes in the performance of the cardiopulmonary resuscitation team members.

Conclusion: The do-not-resuscitate order is informal and exists as a verbal order in the Iranian healthcare system. Also, factors such as the patient's prognosis, pain and suffering, and family members' suffering during and after the resuscitation, and physician characteristics influence the do-not-resuscitate order. On the other hand, this order can reduce the motivation and efforts by healthcare providers to resuscitate patients. The illegal identity of this order creates many challenges for healthcare professionals. Therefore, there is a need to the development of a national guideline based on the Iranian cultural and religious factors. Such a guideline helps with the clarification of the do-not-resuscitate order, which is required to respect the rights of patients and their families and provide legal support to healthcare professionals during cardiopulmonary resuscitation.

Keywords: Cardiopulmonary Resuscitation; Resuscitation Orders; the Do-Not-Resuscitate Order; Content Analysis

■ Clinical Trials and Research in Cancer Nursing

Dr Massey Nematolahi, Dr Rahim- Canada

Abstract

The problem with cancer is that it kills people and greatly diminishes quality-of-life) QoL .(Cancer clinical trials are the key to remarkable improvements in both survival and QoL .Participation in the clinical trials in most of the cancer centers are limited due to lack of research infrastructure and research-trained nurses to work on the trials .Clinical research trials are the backbone of scientific advances against cancer .In this workshop the essential role of clinical trials was described in order to advance cancer care ,explore patient perspective on the value of clinical trials ,and differentiate between prevention ,therapeutic study designs ,and QoL – supportive care designs .The study also described the research phases of clinical trials including purposes and limitations.

Common barriers to research program planning were identified and techniques to improve community awareness ,and recruit-

ment strategies discussion were the last part to wrap up the workshop.

■ Investigation of Frequency, Severity, and Symptoms Distress in Patients With Leukemia Admitted to Hematology and Oncology Wards of the Selected Hospitals in Isfahan, Iran, 2016

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Abstract:

Introduction: Symptom management is an important caring issue among patients with leukemia. However, still little attention is paid to assess symptoms in this group from different aspects (frequency, severity, and distress).

Methods: The current cross sectional study enrolled 400 patients with different types of leukemia in Alzahra, Seyyedalshohada, and Hojjatiyeh hospitals by the convenience sampling method in Isfahan city, Iran, in 2016. A demographic questionnaire and memorial symptoms assessment scale (MSAS) were employed to collect data. Descriptive analysis was performed using SPSS software version 20.

Findings: According to the current study results, the most common symptoms experienced by more than 50% of patients were: lack of energy, difficulty with sleeping, feeling of sadness, pain, being nervous, feeling drowsy, worry, irritability, loss of appetite, numbness and tingling in hands and feet, weight loss, sweating, and dry mouth. Also, the most common symptoms base on frequency, severity, and distress were worry, lack of energy, pain, difficulty with sleeping, feelings of sadness, being nervous, and irritability, respectively.

Conclusion: Results of the current study showed that psychological symptoms were greater than the physical symptoms experienced by patients with leukemia. Thus, psychological support and counseling are necessary for such patients.

■ Physical Needs of Adolescents With Cancer: A Qualitative Research

Dr. Masoud Bahrami, Parastoo Oujian, Dr. Mahboobeh Namnabati, Dr. Fariborz Mokarian

Abstract:

Introduction: Today cancer is a major health issue focused worldwide. Although incidence of cancer is 2 times more in adolescents

than children, their specific needs remain scarce. The current qualitative article aimed at discovering the physical needs of adolescents with cancer within the age range of 15 to 20 year.

Method : It was a descriptive ,exploratory ,qualitative study in which 33 participants were interviewed) adolescents with cancer as well as their parents ,and health care providers .(Data were analyzed by the constant comparison analysis method.

Findings : Analyzing data yielded 4 main categories :need for energy management ,need for nutrition management ,need for physical side effects management ,and need for fertility consultation.

Conclusion: Adolescents and young adults with cancer aged 15 to 20 years emerged as a distinct group requiring specialized care .Cancer had significant impact on different aspects of their lives especially the physical one .This challenge needs more attention and intervention of health care professionals.

Keywords: Adolescents With Cancer; Physical Needs; Parents; Health Care Providers

■ Challenges for Iranian Oncology Nurses

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Abstract:

Nursing is an integral part of the health care system. The professional oncology nurses significantly contribute to patients' well-being and clinical outcomes, particularly nowadays; the role of the oncology nurse is expanding to a more specialized manner. Iranian oncology nurses face many limitations and barriers such as shortage of qualified staff and equipment.

Expanding the role of oncology nurses is imitated due to lack of specialized education and training for nurses in cancer care. While nurses are eager to be engaged in cancer care, the nurses do not have specific training in the field of cancer care. However, the current curriculum prescribed by the nursing schools of Iran is basic and undergraduate nursing education contains very minimal aspects of oncology nursing.

Iranian oncology nurses should be well prepared for their job and expanding their role as the tumor specific clinical nurse specialists. The establishment of oncology nursing society, as well as oncology nursing forum facilitates and develops the active roles of nurses in cancer care

■ Association of Genetic Variants in ABCB1/MDR1 With Poor Prognosis in Patients With Esophagus Squamous Cell Carcinoma

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Abstract:

Background: Esophageal cancer (EC) is highly prevalent and among the leading causes of death in the developing countries. ATP-binding cassette superfamily (ABC) is involved in transferring drugs, detoxification, regulation of protein synthesis, and cell resistance. Rs2032582, a tri-allelic missense variant on ABCB1 gene, is associated with drug resistance. The current study aimed at exploring the association between ABCB1 rs2032582 with ESCC for the first time in 376 patients with and without ESCC.

Method: DNAs were extracted from ESCC samples and genotyped by TaqMan real-time polymerase chain reaction (PCR). The Kaplan-Meier was applied to analyze overall survival and progression-free survival followed by log-rank to compare the data. Logistic regression was utilized to assess the relationship between the prognosis of ESCC and genotypes.

Result: The study data showed that patients with ESCC had a higher frequency of a T/A (TT/TA/AT/AA) genotype for rs2032592 than individuals with GG-genotype. There were no associations between patients' body mass index (BMI) and genotypic frequencies. Furthermore, patients with TT/TA/AT/AA genotype had poor survival (P=0.02) and disease-free survival (P=0.016) in comparison with GG genotype.

Conclusion: The current study demonstrated the significant association of ABCB1 rs2032582 with the prognosis of ESCC, although the possible influence of dietary intake and habit cannot be excluded.

Keywords: Esophagus Squamous Cell Carcinoma; ABCB1; rs2032582, Malnutrition

■ A Comparative Study of Face-to-Face Education and Written Training on Patients With Cervical Cancer Candidate for Brachytherapy in a Six-Month Period From April to October 2016 at Imam Khomeini Hospital in Tehran

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Abstract:

Background: Patient education, part of the broader field of health education, is known as a process through which people learn to take care of their own health and society .The current study aimed at determining the effect of face-to-face education and that of written teaching on patients' anxiety and satisfaction with the provided services.

Materials and methods: The current study was performed on 2 groups of 20 females with uterine cancer who were candidates for brachytherapy in Imam Khomeini Hospital in Tehran. Educational intervention in the first group was designed in the form of a training pamphlet. Educational intervention in the second group was in the form of a 20-minute training session during the pretreatment meeting and in full compliance with the first form of instruction aimed to investigate the effect of the 2 educational methods on the level of anxiety and satisfaction in patients.

Patients` anxiety was measured in both groups in 3 stages of before, mid-session, and 1 month after treatment using the Spielberger standard questionnaire (STAI). Patients' satisfaction with education was evaluated using the visual analogue scale (VAS), 1 month after the treatment. Data were analyzed with SPSS version 22 using the repeated measurement ANOVA and the paired t test.

Results: Statistical analysis of the 2 groups showed no significant relationship between the 3 levels of apparent anxiety (before treatment, midterm treatment and 1 month after treatment) ($P>0.05$). In the study of hidden anxiety in both groups at 2 levels (before treatment and 1 month after treatment), there was no significant relationship between the amount of post-training anxiety ($P>0.05$).

In comparison between the patients' satisfaction and the services provided, the second group, with respect to MI, was more satisfied than the first group, and there was a significant relationship between the type of education and satisfaction ($P<0.001$).

Conclusion: Face-to-face education has a much more positive effect on cancer patients in order to increase the satisfaction with the provided services, depending on the level of communication with the patient. However, this method alone does not affect the patients' anxiety.

Keywords: Face-to-Face Education; Written teaching; Anxiety; Satisfaction

■ Investigation of the Relationship Between Insulin Genes (INSR rs 1799817) and the Risk of Colorectal Cancer in Males

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Abstract

Background: The insulin gene is involved in the process of cellular death by connecting to specific receptors and half of the insulin structure is similar to that of the growth factor that augments the cell growth and proliferation message. One of the polymorphisms associated with the genes involved in colon cancer is the insulin signaling pathway. The current study aimed at examining the relationship between insulin genes (INSR rs 1799817) and the risk of colorectal cancer in males.

Method: The current study included 130 males with intestinal cancer and 120 controls. DNA extraction was carried out using the salting out method. Then, the sequence was amplified by polymerase chain reaction (PCR), and finally, the specific sequence was cut with restriction fragment length polymorphism (RFLP) technique.

Results: The prevalence of T mutant allele was 32.7% in the patient group and 24.3% in the control group, indicating no significant association between the 2 groups in terms of allele frequency (odds ratio (OR) =1.62; 95% confidence interval (Cl) =1.2-2.43). The OR for homozygous mutants was also calculated as follows: normal homozygote (OR = 0.62; 95%Cl=1.4-1.43) and heterozygote versus normal homozygote (OR95% 21.31 / 13.1.19).

Conclusion: There was no significant relationship between insulin gene polymorphism (INSR rs (1799817) and the risk of colon cancer based on the results. Of course, the study of other factors associated with this gene suggests the incidence of the disease.

Keywords: Insulin; Colon; PCR; RFLP; Polymorphism

■ A National Survey of the Availability of Advanced Radiation Technology in Iran, in Comparison With Some other Developed and Developing Countries

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Abstract

Background: According to the World Bank, Iran is in the upper middle income category similar to Turkey. Iran is the second largest economy in the Middle East and North Africa (MENA) region after Saudi Arabia. Iran's GDP in 2016 was $US 412 billion. Implementation of advanced radiation technologies including IMRT is a challenge in Iran, both in terms of optimal treatment and health resources.

Method: During 2015, data of all radiation oncology centers countrywide were collected using a questionnaire regarding the availability of advanced radiation technologies. The variables pertained to 4 important components: intensity-modulated radiotherapy (IMRT), image-guided radiation therapy (IGRT), stereotactic radiosurgery (SRS), and stereotactic body radiation therapy (SBRT). Results were compared with those of some other developed and developing countries.

Results: In 2015, fifty-four fully operational external beam radiotherapy centers were identified in Iran. Among these centers, 3-dimensional conformal radiotherapy (3D-CRT) was available in 52 (96%) centers. IMRT was available in 2 (3%) centers and SRS in 1 (1.85%) center. Also, intraoperative Radiotherapy (IORT) was available in 2 (1.85%) centers. The main barriers to implement advanced radiation technologies included lack of equipment, treatment planning software, and trained personnel.

Table 1: Comparison of Iran with some countries in terms of the use of advanced radiotherapy technologies

Country	Year of Study	IMRT USE	SRS USE	SBRT USE	IGRT USE
Iran	2015	3%	1.58%	0%	10%0 0%[a]
Canada[1]	2010	87%	42.5%		
United States[2,3,4]	2004	73.2%/2004		63.9%/2011	93.5% 82.3%[a]
Australia[5]	2013	37%			86% 50.5%[a]
Turkey[6]	2014	40%			40%
Hungary[6]	2014	4%			9%
Japan[8]	2012	32.6%			42.8%

a; When the use of megavoltage (MV) portal imaging was excluded from the definition of IGRT.

Conclusion: The demand for advanced radiotherapy technologies is steadily increasing in Iran. However, the gap between available facilities in Iran and developed countries is significant.

■ A Meta-analysis of Sodium Iodine Symporter Gene Promoter Methylation in Thyroid Cancer

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Abstract

Promoter methylation in a number of tumor suppressor genes (TSGs) can play crucial roles to develop thyroid carcinogenesis. The current meta-analysis aimed at determining the impact of 8 selected candidates TSGs promoter methylation on thyroid cancer and identifying the most important ones in this carcinogenesis pathway. Comprehensive search was conducted on PubMed, Scopus, and ISI Web of Knowledge and eligible studies were included for the next steps. The methodological quality of the included studies was evaluated according to the Newcastle-Ottawa scale and the pooled odds ratios (ORs), and concurrently 95% confidence intervals (CIs) were considered to estimate the strength of the associations using Stata 12.0 software. The Egger and Begg tests were applied to detect the publication bias, in addition to metatrim. A total of 55 articles were selected and 135 genes were found with checked promoter methylation alterations. Finally, 8 tumor suppressor genes (TSGs) were included in the meta-analysis found in more than 4 studies as follow: RASSF1, TSHR, PTEN, SLC, DAPK, P16, RARb2, and CDH1.The order of the pooled ORs for these 8 TSGs from higher to lower significant values were CDH1 (OR=6.73), SLC5 (OR=6.15), RASSF1 (4.16), PTEN (3.61), DAPK (OR=3.51), P16 (OR=3.31), TSHR (OR=2.93), and RARβ2 (1.50). The publication bias and sensitivity analysis confirmed the least possible bias in the current study. With regard to the current study results, CDH1 and SCL5A8 genes were more important than other genes as a risk factor for thyroid tumor genesis.

Keywords: Tumor Suppressor Genes; Methylation; Thyroid Cancer

■ Demographic Characteristics and Trends in Referral of Patients With Laryngeal Cancer to the Radiotherapy and Oncology Department of Ahvaz Golestan Hospital, Iran, From 2001 to 2012

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Abstract:

Background: Laryngeal cancer is a common malignancy of

upper airway with different oncological treatments such as laryngectomy, laryngectomy and adjuvant (chemo) radiotherapy, definitive (chemo) radiotherapy, and palliative treatment for metastatic cases.

Objective: The current study aimed at evaluating the type of above mentioned treatments in patients with laryngeal cancer referred to Radiotherapy and Oncology Department of Ahvaz Golestan Hospital, Ahvaz, Iran, from 2001 to 2012.

Methods: The current descriptive retrospective epidemiological study included all patients with laryngeal cancer referred to the department of radiotherapy and oncology during the study period. All patients with laryngeal cancer were included if they had a complete documented data.

Results: A total of 490 patients with laryngeal cancer were included in the current study. The results of the study showed that the prevalence and percentage of the patients with laryngeal cancer (relative to the total cases of laryngeal cancer) significantly increased (p-value=0.01), but the percentage of the patients with laryngeal cancer (relative to all of the patients in the radiotherapy department) had a significant decreasing trend (p <0.001).The rarest age ranges were less than 20 years, 20-30, and 90-100 years and the most common age range was 60-70 years. Totally, 438 patients were male (89%) and 52 (11%) female; 60% of patients were referred for definitive therapy and larynx preservation. Out of the 37% of the patients referred for the adjuvant therapy, only 33% received adjuvant therapy and 4% did not require it; 3% of the patients were referred for palliative therapy. It seems that none of the treatments had statistically significant change during the study period. In addition, the percentage of total laryngectomy had no significant change in these years.

Conclusion: The current study showed that despite the global trend of increasing interest in the use of therapies to preserve the larynx, in Iran still a large number of patients are referred to the radiotherapy department after laryngectomy for adjuvant therapy and are deprived from the advantages of laryngeal preservation by the modalities such as radiation therapy with concurrent chemotherapy and definitive radiotherapy.

■ Comparison of Disease Free Survival in Lymph Node Positive Breast Cancer Cases Based on Metastatic Lymph Node Ratio

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Abstract:

Objective: The prevalence of breast cancer varies among countries and regions. Metastasis to the axillary lymph nodes (LN) is a key indicator of prognosis in breast cancer. The current retrospective study aimed at investigating the prognostic value of the metastatic lymph node ratio (MLNR) compared with other clinicopathologic factors in Iranian patients with breast cancer.

Methods: The current retrospective study was performed to evaluate the prognostic significance of MLNR compared with other factors (age, N stage, T stage, hormone receptor status, grade, HER-2 over expression, and LVI) in a cohort of LN positive breast cancer cases. The medical records of 563 female patients treated in the Oncology Department of Jorjani Center from 1997 to 2006 were reviewed and analyzed.

Statistical analyses were performed with SPSS version 19. The Kaplan-Meier analysis with log-rank test was used to determine 5-year disease free survival (DFS) curves. Univariate and multivariate Cox proportional hazards analyses were performed to identify prognostic value of MLNR and other clinicopathologic factors in patients with node positive breast cancer.

Results & Conclusion: The cutoff point of 0.19 was defined for MLNRs and divided patients into those with low- and high-risk groups in terms of 5-year DFS. These 2 MLNR groups had significantly different 5-year DFSs, and MLNR was more accurate than other parameters to predict DFS. The current study findings supported the use of MLNR as a predictor of 5-year DFS in patients with node positive breast cancer, and that MLNR was superior to other factors in determining prognosis.

Keywords: Breast Cancer; Disease Free Survival; Metastatic Lymph Node Ratio

■ Evaluation of Dose Calculation Algorithms of Eclipse and PCRT Treatment Planning Systems Using IAEA TPS Commissioning

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Abstract

Introduction: Radiation therapy is one of the important methods to treat various types of cancer. The accuracy of dose calculation is crucial to the quality of treatment planning and, consequently, to the delivered dose to patients undergoing radiation therapy. There are uncertainties in the calculation of dose distributions, especially in the presence of heterogeneous media. The current study aimed at assessing the accuracy of 3 dose calculation algorithms on tissue inhomogeneity corrections, including Clarkson (Clkr), superposition (SP), and anisotropic analytical algorithm (AAA).

Materials and Methods: A heterogeneous phantom was scanned using computed tomography (CT) images and all of

the tests were planned on 3-dimensional treatment planning systems (TPSs) using the IAEA TPS commissioning .All tests were performed using a 6 MV photon beam of a Varian linear accelerator and ionization chamber .The deviation between measured and TPS calculated dose was reported .This methodology ,which employed the same phantom and the same set of test cases ,was tested in one hospital using 3 different algorithms/inhomogeneity correction methods implemented in different TPSs.

Result : In the homogeneity media ,all algorithms showed good accuracy and dose difference was low ,but in the presence of inhomogeneity ,dose differences increased and in some cases did not achieve agreement criteria .According to the obtained results ,the largest deviation when lung was in the field ,for AAA ,and SP algorithms ,were 7.5% and 10.6% respectively .In addition ,for AAA algorithm when lung was out of filed ,up to 8.9% underestimation was observed .However ,AAA and SP had better accuracy .The Clarkson algorithm had maximum differences ,especially in lung inhomogeneity.

Conclusions : The accuracy of dose calculation algorithms in treatment planning systems is different .Model-based algorithms have a good accuracy over correction-based algorithms such as that of Clarkson .The advanced algorithms are more desirable and therefore should be implanted in clinical practice, especially for calculation in inhomogeneous media such as those of lung and bone.

Keywords: AAA algorithm; Clarkson Algorithm; Superposition Algorithm; Photon Dose Calculation; Treatment Planning System

■ **Monte Carlo Verification of Experimental Virtual Electron Source Position**

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Abstract

Background: Determination of the appropriate dose distribution in tumor region in treatment with the electron beams depends on exact verification of the distance between virtual electron source position and the patient's body. The current study aimed at finding the effective source–surface distance (SSD) using the Monte Carlo (MC) method to substitute the measurements in the clinic.

Materials and Methods: The MC simulation of ONCOR linear accelerator (LINAC) was done based on manufacturer's data in 9-MeV electron beam energy. In order to obtain the values of effective SSD using the inverse slope technique, the water phantom was simulated in the standard SSD, then the simulations were done with an increasing air gap of 3, 6, 9, and 12 cm between the distal end of the applicator to the surface of the water phantom, then surface point doses inside the water phantom model were calculated at dmax in each of the simulations.

Results: To validate the current study simulation results, the MC-calculated effective SSDs values in a water phantom were compared with those of the experimental data measured in the current study as well as with those of other works. The effective SSDs were 95.68 and 96.66 cm from the MC tallies of *F8 and *F4, respectively. In addition, the effective SSDs were 95.59 cm from the ion chamber.

Conclusion: Based on the results obtained from 3 methods of calculation, and comparing them with those of the experimental methods, it was observed that MC simulation was a useful method to determine electron virtual source position.

Keywords: Electron Beam; Effective SSD; Virtual Source Position; MCNP5

■ **The 2D-dose Reconstruction by Artificial Neural Network for Pretreatment Verification of IMRT Fields**

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Abstract

Purpose: The use of intensity modulated radiation therapy (IMRT) is developing rapidly in clinical routine. Due to the high complexity and uniqueness of IMRT treatment plans, patient-specific pretreatment quality assurance (QA) is generally considered a necessary prerequisite to treat patients. The current study aimed at proposing a new methodology of electronic portal imaging device (EPID)-based dose validation for pretreatment verification of IMRT fields by applying artificial neural networks (ANNs).

Methods: The ANN should be trained and validated before use to verify pretreatment dose. For this purpose, 20 EPID fluence maps of anterior-posterior (AP) prostate IMRT field were used as an input for ANN (feed forward type) and a dose map of those fluence maps predicted by TPS as an output for ANN.

Results: After the training and validation of the neural network, the analysis of 10 IMRT prostate AP fields showed excellent agreement between ANN output and dose map predicted by TPS. The average overall field pass rate was 96.0% ± 0.1% with 3 mm/3% criteria.

Conclusion: The results indicated that the ANN can be used as a low-cost, rapid, and powerful tool for pretreatment dose verification, based on an EPID fluence map.

Keywords: Artificial Neural Network; Electronic Portal Imaging Device; Dose Verification; Intensity Modulated Radiation Therapy

ABSTRACT

■ Beam Penumbra Width Determination of Gamma Knife Machine Model 4C Using Monte Carlo Simulation

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Abstract

Gamma knife stereotactic machine is used to treat intracranial disorders using 201 ^{60}Co sources. Beam penumbra is one of the most important beam features that must be considered in the treatment planning due to the exposure of healthy tissue adjacent to the tumor to radiation. In the current study, the EGSnrc/BEAMnrc was used to simulate Gamma Knife model 4C. Single beam and 201 beams profiles were obtained using EGSnrc/DOSX-YZnrc code to determine beam physical penumbra width (90%-50%). All profiles were measured using EBT3 films at isocenter depth in a Plexiglas head phantom. According to the results, the single beam penumbra widths from simulation data for 4, 8, 14, and 18 mm collimator sizes were 0.785, 0.790, 0.82, and 0.904 mm, respectively. Beam penumbra width increased by increasing the field size. The penumbra width of 201 beams was worse than single beam penumbra width due to penumbra overlap. The 201 beams, physical penumbra widths (90%-50%), were 1.2, 1.8, 2.5, and 2.9 mm from simulation and 1.4, 2.2, 2.5, and 3.1 mm from film measurement for the field sizes 4, 8, 14, and 18 mm, respectively. Although the differences were in an acceptable range, for more precision due to the difference between measurement and simulation penumbra width in penumbra region that dose gradient is high, the use of Monte Carlo simulation is recommended for radiosurgery fields penumbra evaluation.

Keywords: Gamma Knife Model 4C; Monte Carlo Simulation; Physical Penumbra

■ Determination of Therapeutic Standard Field for Patients With Cancer Including the Medical Megavoltage Accelerator

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Abstract

Background and objectives: Accurate calculation of equal square field size is important in radiation therapy and A factor in the Vadash formula should be determined by considering collimator exchange effect. Therefore, the current study aimed at determining the best A factor to calculate equal square field sizes in the treatment planning.

Material and method: A new simple protocol method based on the selection of the best dosimetric data was proposed to obtain A value in Vadash equation to predict its equivalent square field size, which compensates collimator exchange effect in output factors in air (OF_{air}). Measurements were performed with the Farmer chamber 0.6 mL in source–surface distance (SSD) 100 cm and build-up cap of Plexiglas, 1.5 and 3.5 cm equal volumes of water, for 6 and 18 MV, respectively, on a Perimus Plus linear accelerator. OF_{air} was measured for square and rectangular fields. MATLAB software (version R2014a) was used for calculations and curve fitting

Results: Power model with constant value was applied to OF_{air} as a function of square field size. OF_{air} ranged from 0.983 to 1.038 in 6MV and from 0.731 to 1.05 in 18 MV and Y collimator had a greater effect on the OF_{air}. The values of 1.42 and 1.55 were selected for "A" in 6 and 18 MV, respectively.

Conclusion: The proposed A values minimized the collimator exchange effect, in calculating the equivalent squares that play an important role in the patient dose calculation and treatment planning. The value of A should be calculated for each machine and energy.

Keywords: Equal Square Field Size; Collimator Exchange Effect; Vadash Formula; Output Factors in Air

■ Assessment of the Factors Involved in Local Recurrence of Breast Cancer: A Single Institution Study

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Abstract

Background: Numerous studies addressed local recurrence after breast conservation therapy, but the risk factors for the recurrence are poorly investigated. The current study aimed at evaluating the impact of different risk factors on local recurrence of the breast tumors after breast conservation surgery.

Methods: All eligible patients for breast conservation surgery from April 2002 to December 2010 were retrospectively reviewed. Patients' demographics as well as known or potential risk factors for local recurrence including age, stage, tumor type, hormone receptor presence, and history of radiotherapy/hormone therapy were considered.

Results: Out of the total 153 patients, 115 completed the study follow-up period for at least 24 months. The study results showed that young age (<40 years) at diagnosis was an independent predictive factor for local recurrence in females treated with breast conservation surgery. In the current retrospective study, cumulative local recurrence rate of 9.6% was reported for all patients, regardless of their age and other risk factors. Overall survival rate according to the Kaplan-Meier plots for the patients in the follow-up period was 90.4%. Moreover, univariable tests showed that patients <40 years were nearly twice as likely to experience local recurrence (hazard ratio (HR) = 1.98; P = 0.01). This is while estrogen or progesterone receptor positivity and adjuvant radiotherapy decrease the probability of the local recurrence. Multivariable analysis showed that nodal involvement increased the chance for local recurrence.

Conclusion: The current study results were consistent with those of the Western literature that suggests risk factors for local recurrence after breast conservation surgery include age <40 years, node positivity, ER negativity, and absence of adjuvant radiation therapy. Patients under 40 years are at increased risk for local recurrence after breast conservation surgery.

Keywords: Breast Conservation Therapy; Local Recurrence; Risk Factors; Survival

■ Androgen Receptor in Breast Cancer With Negative Estrogen Receptor

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Abstract

Introduction: Nowadays the prognostic role of hormonal receptor including estrogen and progesterone in breast cancer is known. But, about one-third of patients with breast cancer have negative estrogen receptor and there is no possibility for hormonal therapy for them. The current study aimed at evaluating the prevalence of androgen receptor in patients with breast cancer and negative hormonal receptors.

Materials and methods: The current historical cohort study was conducted on patients with breast cancer referred to the Clinical Oncology Department of Imam Hussein Hospital from 2010 to 2012; a total of 61 patients with negative estrogen receptors breast cancer were included. Data collection was conducted based on the patients' medical records. The androgen receptor status was evaluated by immunohistochemistry.

Findings and conclusion: According to the results of the current study, 42.6 % of the patients with negative hormonal receptor breast cancer had positive androgen receptor. According to the rate of positive AR in Iranian patients, more studies can be designed on antiandrogen treatment.

Keywords: Breast Cancer; Androgen Receptor; Estrogen Receptor

■ Outcomes of Definitive Chemoradiotherapy for Cervical and Upper Thoracic Esophageal Cancers; a Single Institution Experience of a Rare Cancer

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Abstract

Background/Aims: Upper esophageal carcinomas are uncommon, but confer a poor prognosis. However, there is scarcity of data regarding the outcomes of definitive radiochemotherapy for cervical and upper thoracic esophageal squamous cell carcinoma (SCC) in Iran.

Material and Methods: The current retrospective, cohort study analyzed data of patients with SCC of cervical and upper thoracic esophagus (16 to 25 centimeters from incisors) treated by definitive radiochemotherapy in the under study institution from 2007 to 2015. The primary outcome was overall survival and the secondary outcomes were predictors of overall survival.

Results: From 2007 to 2015, a total of 40 patients entered the final analysis. The mean age of patients was 59.7±14.3 years (range: 24-85). Sixteen patients (40%) were node positive. The median follow-up time was 15.3 months. Twenty-seven patients (67.5%) died during the posttreatment period; 35% and 25% of the patients had local and distant recurrences, respectively. The actuarial median overall survival was 19.2 months (95% confidence interval (CI): 14.2-24.2). The 1- and 2-year overall survival rates were 76% and 38%, respectively. The overall survival was higher among patients under 50 years old, female, stage II, grade 1 or 2 that received induction chemotherapy and treated with doses <60 Gy. However, none of the differences was statistically significant.

Conclusion: Cervical and upper thoracic esophageal SCCs are associated with bad outcome. Studies with large sample sizes are required to define best treatment strategies.

Keywords: Esophageal Neoplasms; Chemoradiotherapy; Survival; Iran

■ Acute Toxicity Profile of Concomitant Chemoradiotherapy in Head and Neck Cancers; a Randomized, Controlled, Comparison of Weekly versus Triweekly Cisplatin Schedule

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Abstract

Aim: The standard chemoradiotherapy (CRT) protocol in head and neck cancers (HNC) consists of 3 cycles of high-dose cisplatin once every 3 weeks. However, due to the significant toxicity and poor compliance of this regimen, with the assumption that more frequent administration of smaller doses of cisplatin during the RT course will minimize adverse effects without compromising treatment efficacy weekly cisplatin schedules were developed. The current study aimed at evaluating and comparing the acute toxicity profiles of these 2 concomitant CRT protocols in squamous cell carcinoma of the head and neck.

Method: For this purpose, 89 patients with HNC considered as CRT candidates, were enrolled in the trial and randomly assigned into the following 2 groups: 47 patients to arm A (40 mg/m2 weekly cisplatin) and 42 patients to arm B (100 mg/m2 triweekly cisplatin). According to the National Cancer Institute (NCI), Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, weekly assessment and grading of acute toxicities was done.

Result: The current study results did not show any statistically significant difference between the rate of treatment interruption and acute hematologic and non-hematologic toxicity profiles of the 2 schedules of cisplatin administration. There was only a trend of grade 3 and above mucositis in the weekly cisplatin arm, but it did not reach a statistical significance.

Conclusion: In conclusion, weekly administration of cisplatin concomitant with radiotherapy had no advantage over every 3-week schedule in terms of acute treatment toxicity; thus, it cannot be routinely recommended.

Keywords: Toxicity; Cisplatin; Chemoradiotherapy

■ Pathological Diagnostic Pitfalls in Brain Tumors; Can Imaging Lead to Pathology Alternation?

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Abstract

Introduction: Pathological diagnosis of brain tumors is very challenging. The current study aimed at evaluating the discordance between imaging data and pathological diagnosis of brain tumors.

Method: The current descriptive study assessed the medical records of patients who referred to neurooncology clinics of Omid and Emam Reza hospitals, Mashhad University of Medical Sciences, Mashhad, Iran from 2009 to 2010. The study aimed at evaluating the correspondence between pathological and imaging findings, and also reviewing the lams in case of discordance.

Result: Imaging/pathological discordances were found in 11 out of 240 patients (4.5%), which in 82% of the patients was associated with diagnosis alternation.

Discussion: The current study showed that imaging/pathological discordances exist and is associated with management alternation. Treatment approach and prognosis of patients with brain tumors substantially vary across different subtypes and grades. Considering the limited sources in developing countries such as Iran, reviewing the pathological findings of patients is not practical. Therefore, the study suggests the familiarity of all 3 main arms involved in the treatment of brain tumors (i e, neurooncologists, neurosurgeons, and pathologists) with corresponding issues.

Keywords: Pathology; Radiology; Brain Tumors Verification

■ Thyroid Dose and Hypothyroidism as a Result of Radiation Therapy for Head and Neck Malignancies and Brain Tumors in Iran

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Abstract:

Radiation therapy has a fundamental role in the treatment of cancer. The goal of this treatment modality is to achieve tumor control probability (TCP) while avoiding normal tissue complication. The sensitivity of the thyroid gland to radiation increases the risk of developing secondary thyroid cancer and hypothyroidism. The average dose to the thyroid from head and neck irradiation was measured using in vivo dosimetry (thermoluminescent dosimeter (TLD). Radiotherapy was performed using 6 MV x-rays from an Elekta compact linear accelerator and conformal radiation therapy was also delivered 1.8 to 2.0 Gy over 5 sequential days per week. The average absorbed dose to the thyroid from head and neck radiotherapy was 4.4% of the prescription dose and from whole brain radiotherapy was 0.7% of the prescription dose. Thyroid stimulating hormone (TSH) levels were determined in 30 patients before and after completion of radiation therapy. The average concentration of TSH increased from 0.88 ±0.55 (preradiotherapy) to 1.7 ± 0.66 mIU/L (postradiotherapy) (P <0.05). Thyroid absorbed dose was less than the threshold dose for patients who received radiotherapy to the head and neck based on thyroid function tests.

Keywords: Radiotherapy; Hypothyroidism; Thermolumincsence dosimetry; Treatment Planning System; Head and Neck Tumors

ABSTRACT

■ The Methodological Quality Assessment of Extant Clinical Practice Guidelines in Cancer Therapy-induced Mucositis; a Systematic Review

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Abstract:

Introduction: Oral mucositis is a common complication in patients with cancer therapy. Oral and dental care should be considered as a vital component of caring before, during, and after chemotherapy. The current study aimed at assessing the methodological quality of the existing CPGs (clinical practice guidelines) about cancer therapy-induced mucositis.

Method: A systematic review of the extant of CPGs was conducted to manage mucositis. After screening the guidelines based on the inclusion and exclusion criteria, 3 CPGs were selected and assessed by 5 appraisers using the AGREE (the appraisal of guidelines for research and evaluation) II instrument. Intraclass correlation coefficient was used for inter-rater reliability. SPSS version 11.0 software was used for data analysis.

Results: The assessed CPGs gained the highest scores in the clarity of the presentation domain. Scope and purpose (median score= 63.3%) as well as stakeholder involvement (median score= 54.4%) were found respectively and the lowest scores belonged to the editorial independence domain. The scores in applicability (median score= 30%), rigor of development (median score= 28.8%), and editorial independence (median score= 26.7%) domains were unfavorable. Also, every appraiser scored the overall quality of CPGs.

Conclusion: The quality of mucositis CPGs needs to be improved. In other words, designing high-quality CPGs in this area is necessary.

Keywords: Mucositis; AGREE II Instrument; Clinical Practice Guidelines

■ Improvement of Dose Distribution Using the Involved-field Radiation Therapy Technique in Hodgkin Radiotherapy

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Abstract:

Background: Almost 75% of patients with Hodgkin lymphoma (HL), regardless of disease stage, have long-term survival after treatment. Radiotherapy with large mantle-field is an effective technique, which increases the risk of secondary cancers among patients with HL; therefore, it is essential to choose an effective treatment with the lowest late complications in radiotherapy. The present study aimed at planning separate fields for neck and mediastinum using various energies in order to compare dose distribution of modifying mantle field with a multileaf collimator (MLC) and block.

Materials and Methods: In the current study, 3D conformal treatments, Siemens ONCOR™ Expression linear accelerator equipped with MLC, were performed to create anterior-posterior fields. Computed tomography (CT) scan data of 18 female patients with neck and mediastinal involvements were entered into the TIGRT (targeted image guided radiation therapy) treatment planning system, and then, the treatment plans were introduced.

Results and Conclusion: The treatment plan 1 was as follows: photon 6 MV in neck weighting 1 from interior, 0.5 from posterior, photon 18 MV in mediastinum weighting 1 from interior and 0.5 from posterior. It was shown that regarding the common treatment plan used with photon 6 MV, the mean dose delivered to breast, lung, esophagus, and larynx reduced 6%, 7%, 41%, and 10%, respectively and uniformity index was improved by 10%. Using block in all treatment plans offered an improved average dose to all organs under study, compared with those of MLC. Using separate fields with Pb blocks, though, showed smaller increase.

Keywords: Treatment Planning; Radiotherapy; Hodgkin; MLC; 3D Conformal Treatment

■ Effect of Mesenchymal Stem Cell-derived Microvesicles on the Differentiation of Hematopoietic Stem Cells From Umbilical Cord Blood to Megakaryocytic Lineage

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ABSTRACT

Abstract

Objective: Mesenchymal stem cells (MSCs) release hematopoietic cytokines, growth factors, and microvesicles (MVs), which support the hematopoietic stem and progenitor cells (HSPCs) in the bone marrow (BM) hematopoietic microenvironment. MVs are the extracellular vesicles releasing from various cells with important intercellular communications, and play a crucial role in the biological functions of their parent cells such as MSC-derived MVs (MSC-MVs). MSC-MVs contain microRNAs and proteins that are rolled in the regulation of hematopoiesis. BM transplantation is a useful procedure in hematologic disorders. Cord blood (CB) is used as a suitable source for transplantation, but the long-time recovery of platelet (PLT) after transplantation is its main problem. Therefore, the current study aimed at showing the potential of MSC-MVs to improve the differentiation of CB-CD34+ cells to MK lineage ex vivo, and indicating the effect of this method on the reduction of thrombocytopenia period.

Materials and Methods: In the current descriptive study, MSCs were cultured in the Dulbecco modified eagle's medium (DMEM) in order to obtain supernatant. The supernatant was ultracentrifuged for the isolation of MVs. Hematopoietic stem cells (HSCs) were isolated from the CB source by the magnetic activated cell sorting (MACS) method. HSCs were cultured in the Iscove modified Dulbecco's media (IMDM) supplemented with cytokines and MVs under 3 conditions. The MK differentiation was evaluated by the specific markers and specific gene expressions after 72 hours. Finally, data were analyzed by the non-parametric t student test (P <0.05).

Results: The expression of MK lineage (CD41/CD61) specific markers showed no significant differences at different concentrations of MSC-MVs, compared with the control group. Also, the specific gene expression of the MK lineage (*GATA1, GATA2, FLI1,* and *c-Mpl*) was normalized with GAPDH (lyceraldehyde 3-phosphate dehydrogenase), as an internal control, compared with that of the control group. *GATA2* and *c-Mpl* expressions significantly increased; *GATA1* expression not significantly decreased, but *FLI1* expression significantly decreased. The results showed no significant improvement of the MK differentiation in response to the synergism effect of MSC-MVs and cytokines.

Conclusion: The results showed that MSC-MVs cannot improve the expression of MK specific genes and improve differentiation rate to the MK lineage. However, further studies on the late stages of the MK differentiation in the culture medium are required to evaluate platelet production and shedding.

Keywords: Microvesicle; Hematopoietic Stem/Progenitor Cell; Mesenchymal Stem Cell; Megakaryocyte

Abbreviation

MSC: Mesenchymal Stem Cell

HSPC: Hematopoietic Stem/Progenitor Cell

HSC: Hematopoietic Stem Cell

MK: Megakaryocyte

Platelet: PLT

MV: Microvesicle

BM: Bone Marrow

mPB: mobilized Peripheral Blood

CB: Cord Blood

GVHD: Graft Versus Host Disease

FBS: Fetal Bovine Serum

PBS: Phosphate Buffer Saline

DMEM: Dulbecco's Modified Essential Medium

SCF: Stem Cell Factor

FL: Flt-3 Ligand

TPO: Thrombopoietin

IL-11: Interleukine-11

Real-time PCR: real-time polymerase chain reaction

■ Absorbed Dose Estimation of [166]Ho-BPAMD as a Potential Agent for Bone Marrow Ablation

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Abstract:

Objectives: In the current study, due to the special properties of BPAMD and importance of the dose received by the target and non-target organs in cancer therapy, the human organs absorbed dose of [[166]Ho]- BPAMD was estimated based on biodistribution data in wild-type mice.

Materials and methods: A stock solution of BPAMD with the concentration of 1 mg/mL in distilled water was prepared and a certain amount of it was added to a vial containing [166]HoCl3. The pH of the reaction mixture was adjusted to 5-6 and the mixture was incubated for 45 minutes at 90-100°C. The radiolabeled compound was injected to mice through the tail veins. Then, 5 mice were sacrificed at certain intervals and the percentage of the injected dose per gram of each organ was measured by counting the activity of each organ. The Medical Internal Radiation Dose (MIRD) formulation was applied to extrapolate from mice to human and to project the absorbed radiation dose of various human organs.

Results: The highest human organs absorbed dose of [166]Ho-BPAMD was measured at bone surface and red marrow 0.916 and 0.647 mSv/MBq respectively. Other organs received an insignificant dose that was the main advantage of the assessed compound.

Conclusions: The results showed that [166]Ho-BPAMD is a suitable and safe agent for bone marrow ablation with high bone uptakes and can deliver large amounts of dose to the bone marrow compared with those of similar bisphosphonate compounds.

Keywords: Absorbed Dose; Ho-166, BPAMD; Bone Marrow Ablation

■ Structural Study and Preparation of [153]Sm-labelled Porphyrin Complex as a Possible Therapeutic Agent

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Abstract:

The current study aimed at assessing the biodistribution activity of [^{153}Sm]-5,10,15,20-tetrakis(phenyl) porphyrin ([^{153}Sm]-TPP) complex as a potential therapeutic agent. For theoretical analysis, geometrical feature and thermochemistry of the complexation reaction were investigated by PM7/SPARKLE semi-empirical quantum mechanics methods. The [^{153}Sm]-TPP was prepared using [^{153}Sm]SmCl$_3$ and 5,10,15,20-tetrakis(phenyl) porphyrin (H$_2$TPP) for 12 hours at 50°C (radiochemical purity: >90±2% ITLC, >95±0.5% HPLC, specific activity: 0.9-1.1 GBq/mM). Stability of the complex was checked in final formulation and human serum for 24 hours. The partition coefficient was calculated for the compound (log P=2.01). The biodistribution of the labelled compound in the vital organs of wild-type rats was evaluated in scarification studies. A detailed comparative pharmacokinetic study was performed for ^{153}Sm cation and [^{153}Sm]-TPP up to 48 hours. The results of computational studies showed that both 1:1 and 1:2 complexes were reliable for Sm/TPP system and the formation of ligand and complexes were exothermic. Also, the biodistribution of the complex in rats demonstrated that [^{153}Sm]-TPP was mostly washed out from the circulation through kidneys and liver. The kidney:blood, kidney:liver, and kidney:muscle ratios 4 hours post-injection were 14, 3.6, and 7.38, respectively. Generally, due to the excellent characteristics of the complex, it can be considered as a good therapeutic agent; however, further biological studies in animal tumor models are recommended.

Keywords: Porphyrins; Quality Control; Sm-153; Biodistribution

■ Importance of Colorectal Cancer Screening in Females With the History of Gynecologic Cancer in Iran

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Abstract:

Background: Colorectal cancer (CRC) is one of the most common types of cancer in Iran. The standardized incidence rate of CRC is 11.1% in Iran. Lynch syndrome (LS) is the most common hereditary form of CRC and causes about 2%-3% of all CRC cases. A study in Iran reported that 3.4% of patients with CRC also had the Amsterdam II criteria and 41.7% met at least 1 criterion for the revised Bethesda guideline. Females with LS are at greater risk for some cancers such as gynecologic (40%-60%) and colorectal (50%-70%) ones. It is not clear that microsatellite instability and/or immunohistochemical analyses are already performed in what proportion of females in high-risk subgroups such as gynecologic cancers. Females with gynecologic cancers and LS are at risk to develop CRC, the second common cancer, 3 times more than their healthy counterparts; this risk is even increases in young females. Gene mutation of LS reported in 2% of ovarian cancer and 9% of endometrial cancer cases. Studies reported that less than half of females with gynecologic cancers were screened for CRC of which 13.6% had significant pathology and 2.4% had colon cancer. Studies reported the predominance left CRC in patients with the history of ovarian cancer and right CRC in the ones with the history of endometrial cancer.
Conclusion: Clinicians should recommend CRC screening for females with gynecologic cancer diagnosed at age under 60 years as well as the ones with tumor diagnosed at 40.

■ Feasibility of Sentinel Lymph Node Biopsy in Clinically Node Positive Breast Cancer Patients With Response to Neoadjuvant Chemotherapy

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Abstract:

Background: Sentinel lymph node biopsy after NAC (neoadjuvant chemotherapy) is controversial especially in clinically node-positive patients; the current study aimed at evaluating the feasibility and accuracy of sentinel lymph node dissection (SLND) in patients with node-negative conversion.
Method: The current prospective, cross sectional study recruited patients diagnosed with breast cancer at Milad Hospital of Tehran, Iran from June 2014 to February 2015. Node-positive patients who underwent NAC demonstrated a node-negative conversion and had a successful SLND (more than 3 SLNs were included in the study). A 2x2 contingency table was used to analyze the feasibility of SLNB (sensitivity, specificity, false negative ratio, and accuracy) in the negative axillary conversion group. STATA statistical software (version 13.0, StataCorp LP, Texas, USA) was used for statistical analyses.
Results: A total of 47 patients enrolled in the study out of which 42.6% were within the age range of 50 to 60 years and 57.4% belonged to 60-70 years age group. In terms of receptors, 55.4% were ER+, 44.8% PR+, and 65.9% Her2+. A sensitivity of 100% (16/16), false-negative rate of 0% (0/21), negative predictive value of 100% (16/16), and overall accuracy of 89.4% were obtained in the present study.
Conclusion: SLND is advisable in breast cancer patients with node conversion, positive hormonal receptors, adequate response to NAC, and successful SLNB with at least 3 SLN dissections during the procedure.

Keyword: Breast Neoplasms; Neoadjuvant Therapy; Sentinel Lymph Node Biopsy; Predictive Value of Tests

■ Radioenhancement Comparison of Gold and Bismuth Nanoparticles in Megavoltage Radiotherapy Using n-PAG Polymer Gel Dosimeter

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ABSTRACT

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Abstract:

Background / Purpose: Recently, considerable researches are in progress on the use of nanomaterials as a new class of radiation sensitizers in radiotherapy (RT). Meanwhile, bismuth nanoparticles (BiNPs) with unique features such as low cost, high atomic numbers, high density, high biocompatibility, and also the minimal toxicity of heavy metals offer significant potential to improve available techniques of radiation therapy. Many of the recent studies focused on dose enhancement properties of gold nanoparticles (AuNPs) during low energy of RT, while destroying deep-lying tumors require much higher energy levels with greater penetration power. Therefore, the current study aimed at investigating the potential of BiNP as the dose enhancer in clinical megavoltage γ-rays, released by cobalt-60 source quantitatively using n-PAG polymer gel dosimeter, and its radioenhancement capability was compared to that of AuNPs.

Material/methods: The BiNPs and AuNPs less than 50 nm in diameter were synthesized. In order to characterize 3 dimensional (3D) dose distribution generated from the interaction between ionizing radiation and the nanoparticles, the n-PAG polymer gel dosimeter was prepared. Tubes containing n-PAG gel were loaded with the concentration of 0.2 mM of synthesized BiNPs and AuNPs and also calibration samples were simultaneously radiated by the cobalt 60 source (1.25 MV). Finally, the radiation-induced polymerization amounts of the irradiated and non-irradiated samples were detected by a Siemens 1.5 Tesla MRI scanner.

Results: The average value of the dose enhancement factor calculated for AuNPs at 0.2 mM concentration was 1.0415±0.28, which decreased to 1.0320±0.37 at the concentration 0.2 mM of BiNPs.

Conclusions: The current preliminary study approved the gold- and bismuth-based nanoparticles in megavoltage RT. Additionally, the n-PAG polymer gel can be employed as a 3D powerful dosimeter to measure and verify the radiosensitization of BiNPs and AuNPs.

Keywords: Bismuth Nanoparticles; External Radiotherapy; Gel Dosimetry; Gold Nanoparticles; Radiosensitization

■ Breast Cancer in Males: a Report From the Department of Radiation Oncology in Kermanshah Province, Iran

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Abstract:

Background: Male breast cancer (MBC) is a rare disease that accounts for less than 1% of all cancers in males and less than 1% of all diagnosed breast cancers. The current retrospective study evaluated the clinicopathological features, treatment options and overall survival in Kurdish MBC cases.

Materials and Methods: Seventeen patients with MBC were referred to the Department of Radiation Oncology in Imam Reza Hospital, Kermanshah, Iran, from 2010 to 2016. Immunohistochemical analysis was performed for ER, PR, and Her2 biomarkers and FISH for the ones with Her2[2+]. Median follow-up period was 30 months (2 to 65 months). The patients not followed up after the initial diagnosis were excluded. Treatment methods were chemotherapy, radiotherapy, hormonal therapy, target therapy, and palliative care. Survival was estimated by the Kaplan-Meier method (Prism 5).

Results: The mean age at diagnosis was 49.24 ± 17 years, ranged 24 to 85. Grade II was the most common grade in MBC (65%). Fourteen patients (82%) had invasive ductal carcinoma, 1 (6%) had ductal carcinoma in situ, and 2 (12%) had invasive papillary. ER, PR, and Her2 were significantly positive in 14, 8, and 2 cases, respectively. The treatment included modified radical mastectomy for most patients. Chemotherapy with TAC (Taxotere, Adriamycin, and cyclophosphamide) and CEF (cyclophosphamide, epirubicin, fluorouracil) regimens were delivered to 15 cases. Tamoxifen therapy was delivered to 14 cases. Three of the stage IV patients received Avastin and 2 with Her2[3+] were given trastuzumab (Herceptin). Patients received adjuvant radiotherapy following surgery and chemotherapy. The site of metastasis was the bone in 2 cases, lung in 1 case, and liver in 1 case. Zoledronic acid (Zometa) was prescribed to patients with bone metastasis. Five-year overall survival rate was 64%.

Conclusions: MBC is rare; thus, larger studies are needed in collaboration with several research centers in the field of breast cancer. ER positive, grade II of invasive ductal carcinoma, stage II, and right-side happen more in patients with MBC. The overall survival in the current study was similar to that of other studies.

Keywords: Male Breast Cancer; Kurdish Iran; Overall Survival ; ER[+]; PR[+]; Her2^{+}; Chemotherapy

■ Survey of Neutrophil to Lymphocyte Ratio as Prognostic Factor in Colorectal Cancer

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Abstract:

Background: Neutrophil-lymphocyte ratio (NLR) is derived from the absolute neutrophil and lymphocyte count obtained from routine complete blood count (CBC). The current study aimed at determining the relationship between neutrophil to lymphocyte ratio and prognostic factors for colorectal cancer.

Material and Methods: In the current study, 70 patients with colorectal cancer were studied according to the research objectives. To compare the NLR with qualitative variables (pathological types), the independent *t* and the Mann-Whitney U tests were used. To assess the correlation with quantitative variables, the

Pearson or Spearman correlation coefficient was used. The significance level was considered 0.05.

Results: Only 4.3% of the patients had a NLR greater than 5 and the mean ± standard deviation (SD) of NLR was 2.1 ± 0.1. Most of the patients were in the age range of 60 to 69 years (31.5%). Mean age (±SD) of the subjects was 60 ± 0.14 years. According to Table 1, females comprised 47.1% of the study patients, while 52.9% were male. The correlation between NLR and the variables grade (P=0.091), T-stage (P=0.527), M-stage (P=0.282), erythrocyte sedimentation rate (ESR) (P=0.386), lymphovascular space invasion (LVSI) (P=0.473), prognostic nutritional index (PNI) (P=0.093), diabetes (P=0.264), body mass index (BMI) (P=0.681), low-density lipoprotein (LDH) (P=0.20), and carcinoembryonic antigen (CEA) (P=0.582) was not significant.

Conclusion: The association between NLR with N-stage (P=0.005) and inflammatory factor (C-reactive protein (CRP) was statistically significant (P=0.016). It is recommended that the evaluation of this factor be considered at the bedside of patients in order to choose the method and treatment and investigate the course of the disease as well as future studies.

Keywords: CRC; NLR; Prognostic Factor; P-value

■ Preparation and Biodistribution Assessment of ^{177}Lu-PSMA-617 in Breast Adenocarcinoma-bearing Mice

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Abstract:

The early diagnosis of the breast cancer to prevent tumor dissemination is highly desirable. In the current study, ^{177}Lu-(2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl) amino] propionylamino}-pentyl)-ureido]-pentanedioic acid) (^{177}Lu-PSMA-617) radiolabeled agent was prepared and its distribution in breast adenocarcinoma bearing mice was studied. The radiolabeled compound was provided with radiochemical purity of higher than 99% at the optimized conditions (15 μg of PSMA; pH 4-4.5 at 90-95°C) and specific activity of 24.4 MBq/μM in about 35 minutes. The complex demonstrated significant stability at room temperature and in human serum at least for 48 hours. Biodistribution assessment in the breast adenocarcinoma-bearing mice showed a major accumulation of activity in the tumor site and the kidneys, as the main route of excretion, at specified intervals up to 168 hours post-injection. The results showed that ^{177}Lu-PSMA-617 has interesting characteristics as a therapeutic agent for breast adenocarcinoma cancer.

Keywords: ^{177}Lu-PSMA-617; Breast Adenocarcinoma; Biodistribution

■ The Frequency of Vitamin Supplement Usage in Patients With Cancer

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Abstract:

Background: There is a tendency to overuse drugs in many people. It is more commonly observed in patients with cancer, especially during or after chemotherapy. The current study evaluated the frequency of vitamin usage in such patients.

Methods: The current study evaluated 200 patients treated with chemotherapy or chemoradiation. They were asked about taking vitamins by themselves or based on the prescription of physician.

Results: Most of the patients were female (59.7%) with the post graduate level of education (48.3%). About one-third (36.3%) had metastatic disease and 43.5% had the history of previous chemotherapy; 20.4% of the patients were treated with chemotherapy alone and 23.7% of the chemoradiotherapy group used vitamins regularly. Patients in their 60's used vitamins more frequently. Interestingly, in 43.9% of the cases the vitamin supplement was prescribed by the physicians. More than half of the patients who consumed vitamin supplements (52.5%) had no medical complication except cancer and had proper nutritional status.

Conclusion: In nearly half of the patients who took vitamins, it was prescribed by the physician during the chemotherapy. As the interaction of vitamins and antioxidants with chemotherapy drugs is not clearly known, it seems prudent to prescribe vitamin supplements only in cases with clear indications to receive such medications.

Keywords: Cancer; Vitamin; Chemotherapy

■ The Comparison Between Different Prostate IMRT Dose Distributions Based on the Cost Function Values in IMRT Optimization Procedure

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Abstract

Introduction: Different radiotherapy centers employ different intensity-modulated radiation therapy (IMRT) techniques, but it is not clear that which technique has better dose distribution regarding to the target tissue prescribed dose and organs at risk (OAR) dose limitations. Due to the different OAR dose limitations and acceptable criteria for target tissue dose distribution among

different centers, it is not possible to compare different techniques employed in different centers. In IMRT planning, there is a mathematical function called cost function, which should be minimized during the optimization procedure. This function illustrates the difference between the planned IMRT dose distribution and the objective dose distribution, and it is dosimetrically better to minimize the cost function value as much as possible in the optimization procedure. The current study aimed at comparing the dose distribution of 4 IMRT techniques based on the cost function values with similar dose limitations and criteria in prostate hypofractionated radiotherapy (70.2 Gy in 26 fractions).

Methods and Materials: Computed tomography (CT) and magnetic resonance imaging (MRI) examinations of 20 patients undergoing prostate radiotherapy with stage ranging T1 to T3b were selected to contribute in the current investigation. After contouring the OARs including rectum, bladder and femur heads, the prostate along with seminal vesicles were contoured as a clinical target volume (CTV). Therefore, 1-1.5 cm margins were considered around the CTV to obtain the planning target volume (PTV). Four IMRT coplanar techniques including 5 fields, 7 fields, 9 fields and beam angle optimization techniques were planned and optimized for each patient in Eclipse treatment planning software. Dose limitations for planning target volume (PTV) and OARs were similar for all patients and techniques in optimization procedure. Cost functions were calculated for each radiotherapy plan dose distribution using the MATLAB R2014b software after the optimization.

Results: The mean value of cost functions for 5-field, 7-field, 9-field and beam angle optimization IMRT techniques were 1.535041, 0.665943, 0.627992 and 0.824564, respectively, for the study patients. Although the 9-field technique had the lowest value among other techniques, the paired sample t test showed no significant difference (P ≤0.05) between the 9-field and 7-field techniques. Other techniques had significant differences with each other.

Discussion and Conclusion: The 9-field IMRT technique had the best cost function compared to others in the current study due to its higher degree of freedom of MLC leaf movements, but it seemed that 7-field technique could provide appropriate dose distributions for prostate IMRT cases. The cost function of 5-field technique had the highest value and was not appropriate for radiotherapy. The beam angle optimization technique needed significantly more time compared to others and its cost function did not have any advantage. Due to higher setup errors (patient and machine positioning) and increase in treatment time for 9-field technique, the 7-field IMRT technique may be the best choice for prostate radiotherapy especially for centers without any Image guiding or adaptive devices. Further researches are required to test other dose limitations and criteria in larger groups of patients with different anatomical structures.

Keywords: Prostate IMRT; Intensity Modulated Radiotherapy; Optimization; Cost Function

■ Comparison of EBT3 Film and Delta4® Measurements to Evaluate the Dose Distribution, Calculated by Eclipse™ TPS in Heterogeneous Chest Phantom Using the IMRT Technique

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Abstract

Purpose: The current study aimed at evaluating the performance of EBT3 film and Delta4® system to measure the dose distribution and compare their results with EclipseTM 3-dimensional (3D) treatment planning system (TPS) in heterogeneous chest phantom using the intensity modulated radiotherapy (IMRT) technique.

Method: Two IMRT plans A and B (were prepared for the radiotherapy of heterogeneous chest phantom in the current study. Plan A was between the left lung and surrounding soft tissue and Plan B was done on the soft tissue. The 95% gamma-index **was** accepted by the criteria of 3mm/3% and the threshold dose of 20 Gy as the standard criteria in the present study. The gamma indices were measured between TPS dose distributions with film and Delta4 and were compared via the Bland-Altman analysis.

Results: The mean gamma-index based on the standard criteria between TPS dose calculations and film measurements was 96.95%, while it was 97.7% and 98.45% between TPS calculations and 2D and 3D Delta4 cases, respectively. The mean 3D gamma analysis of Delta4 based on the given standard criteria was 0.75% that was 1.5% higher than that of 2D gamma analysis.

Conclusion: Both film and Delta4 showed acceptable standard gamma distribution for both plans implemented on the chest phantom using IMRT technique. According to results of the current study, EBT3 films with a simple heterogeneous phantom could be an alternative to evaluate the dose distribution of TPS system in chest region if Delta4 was not available.

Keywords: IMRT; EBT3 Film; Delta4 Phantom; Gamma Index

■ Crocin Synergistically Enhances the Antiproliferative Activity of 5-FU Through Wnt/PI3K Pathway in a Mouse Model of Colitis-associated Colorectal Cancer

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ABSTRACT

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Abstract

Background: Colorectal-cancer (CRC) is the 3rd leading cause of cancer-related-death indicating the need for identification of novel-agents to improve the efficacy of current-therapy. The growing bodies of evidences indicated the antitumor activity of crocin, although its activity and molecular-mechanisms in CRC still remained to be elucidated. The current study explored the therapeutic application of crocin or its combination with 5-fluorouracil (5-FU) in a mouse model of colitis-associated colon-cancer.
Methods: The antiproliferative activity of crocin was assessed in 2- and 3-dimensional cell-culture-models in vitro and in vivo. The migratory behaviors were determined and the expression levels were studied by the quantitative reverse transcription polymerase chain reaction (qRT-PCR) and the Western-blotting techniques. The anti-inflammatory activity of crocin was examined in the current study by pathological evaluations, disease activity index, and antioxidant activity assessment by malondialdehyde (MDA), total-thiols (T-SH), superoxide-dismutase (SOD), and catalase (CAT) activity measurements.
Results: Crocin suppressed cell-growth and invasive-behavior of CRC cells through the modulation of Wnt-pathway and E-cadherin. Moreover, administration of crocin alone or in combination with 5-FU dramatically reduced the tumor number and tumor size in both distal and middle parts of the colon followed by reduction in disease activity score (DAS0. Also, crocin suppressed the colonic inflammation induced by DSS and notably recovered the increased levels of MDA and decreased the activity of CAT/thiol. Crocin could ameliorate multiplicity of severe inflammation with mucosal ulcers and high-grade dysplastic crypts as detected by total score of inflammation, crypt-loss, pathological-changes, and histology-scores.
Conclusions: The current study results demonstrated the anti-tumor activity of crocin in CRC and its potential role in the improvement of multiplicity of inflammation with mucosal ulcers and high-grade dysplastic crypts, which is supporting further investigations on the therapeutic potential of this approach in colorectal cancer.

Keywords: colorectal cancer; crocin; anti-tumor effect; 5-FU, colitis-associated colorectal cancer

■ Radiofrequency Capacitive Hyperthermia Added to Teletherapy as an Alternative to Combination of Teletherapy and Brachytherapy on Human Prostate Cancer Cell Line DU-145

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Abstract

Objective: The current study aimed at evaluating the induced DNA damages of human prostate cancer cells, DU145, in spheroid culture treated with a combination of radiofrequency capacitive hyperthermia and teletherapy compared with a combination of teletherapy and high-dose rate (HDR) brachytherapy.
Material and Methods: DU145 cells were cultured as 300-micron diameter spheroids; then, the following treatments were conducted: a) External beam radiation teletherapy (EBRT) at doses either 2 Gy or 4 Gy of photon 15 MV, b) Hyperthermia (HT) for 30, 60, and 90 minutes at 43°C from a 13.56 MHz radiofrequency capacitive heating device (Celsius TCS), c) Brachytherapy with Ir-192 seed at 2 Gy or 5.5 Gy, d) Hyperthermia followed by teletherapy (HT+EBRT) with 15 minutes intervals, and e) Teletherapy followed by brachytherapy (EBRT+BR). The alkaline comet assay was performed to measure the amount of DNA damage in individual cells as tail moment in response to treatments. The results were delineated as dose-response curves. Consequently, radiobiological iso-effective doses were determined and compared.
Results: Induced DNA damages of DU145 cells showed a significant increase in the cultures treated with HT + EBRT, compared with EBRT alone. A range of doses with radiobiological iso-effects in HT+EBRT and EBRT+BR treatments were found by plotting the dose-dependent curves.
Conclusion: The present study suggested that a significant radiosensitized prostatic cancer cells, DU145, could be obtained by adding hyperthermia to radiation in order to consider HT+EBRT as an alternative to EBRT+BR, partly about induced DNA damages of prostate cancer cells ,and as a treatment of choice for the patients who were the suitable candidates for brachytherapy.

Keywords :Prostate Cancer ;Hyperthermia ;Brachytherapy ;Teletherapy ;Comet Assay

■ Development and Estimation of Absorbed Dose in Human From [47]ScCl₃ and [47]Scandium-Bleomycin as an Antibiotic Tumor Seeking Radiopharmaceuticals

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Abstract

Introduction: The ^{47}Sc is proposed as a potential therapeutic radionuclide and is similar to the clinically established ^{177}Lu. ^{47}Sc is a moderate energy β-emitter with decay characteristics ($T_{1/2}$=3.42d, $E_{\beta max}$= 441 keV ,%68; $E_{\beta max}$= 600 keV ,%32 ; Eγ=159keV) [1] that is potentially useful for radionuclide tumor therapy. Bleomycins are tumor seeking antibiotics widely used in cancer chemotherapy with possible clinical advantages of a combined treatment with irradiation and bleomycin for tumors. The current study aimed at investigating the absorbed dose from ^{47}ScCl$_3$ and ^{47}Sc-BLM in human. Application of radiopharmaceutical distribution and dosimetry across species from small animals such as rats to humans can be useful to accelerate the development of radioactive compounds in clinical settings. Preclinical studies of radiopharmaceutical behavior are useful for predicting pharmacokinetics and their metabolism in humans. In nuclear medicine, the medical internal radiation dose (MIRD) system is the most commonly used method for the calculation and estimation of internal dose [2].

Materials and Methods: In the current study, ^{46}Sc chloride as a substitute for ^{47}Sc was obtained from thermal neutron flux (3 × 10^{13} n.cm^{-2}.s^{-1}) of natural metallic scandium sample followed by dissolution in acidic media, which further used for the labeling bleomycin (BLM), and followed by stability studies as well as biodistribution in mice. ^{46}Sc-BLM was produced as reported in authors' later paper[3]. The animal biodistribution data were extrapolated to the absorbed dose and residence time in human was calculated by the MIRD technique.

Estimation of human dosimetry: The first step in the estimation of human dosimetry was to estimate the percentage of injected activity per organ (%ID/organ) for a certain human organ. This calculation was obtained from animal data by mass correction method as Equation (1). The required mass data for the standard adult male weighing 73 kg were taken from ICRP89[4].

(1)

$$(\%ID)_{human} = \left[\left(\frac{\%ID}{g} \right)_{animal} \times (Kg_{TBweight})_{animal} \right] \times \left(\frac{g_{organ}}{Kg_{TBweight}} \right)_{human}$$

For calculating the residence times (τ), the human absorbed dose was determined by integration of values from t=0 to t=infinity and accounting the physical decay of the ^{47}Sc using the method explained in the MIRDOSE3 code[2, 5].Determination of $\tilde{A}_h$ relied on the residence time (τ)that depended on biodistribution (f: uptake fraction) and retention of radiopharmaceutical in the body (T_e: effective half-life of radiopharmaceutical) and the calculation performed by equation (2).[6-8]

(2)

$$\tilde{A}_h = \int_0^\infty A_h(t)dt = A_0 \int_0^\infty f_s(t)dt = A_0 \times \tau$$

Results: The biodistribution studies of ^{46}ScCl$_3$ and ^{46}Sc-BLM are shown in figures 1&2, and the accumulation of the radiolabeled compounds in lungs, liver, and spleen demonstrates a similar pattern to other radiolabeled bleomycins. Extrapolation of rats %ID/g to human %ID/organ for ^{46}ScCl$_3$ are shown in figures 2&3.The estimation of absorbed dose in human (Table1) showed the effective dose delivery. The absorbed doses of ^{47}Sc-BLM to whole body, red marrow, kidneys, liver, and bone were 0.0072, 0.0086, 0.0084, 0.0153, and 0.0113 mGy/MBq, respectively.
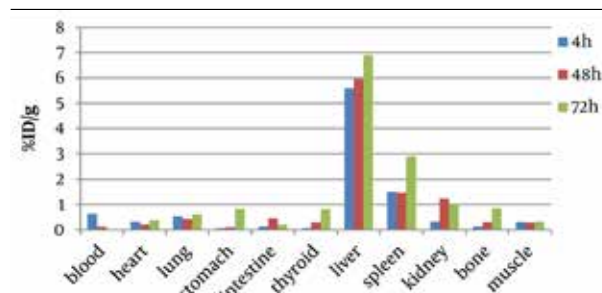
Figure1. Biodistribution of ^{46}ScCl$_3$ in Wistar rats
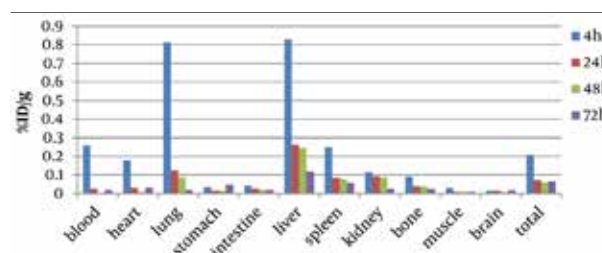
Figure 2. Biodistribution of ^{46}Sc-BLM in Wistar rats
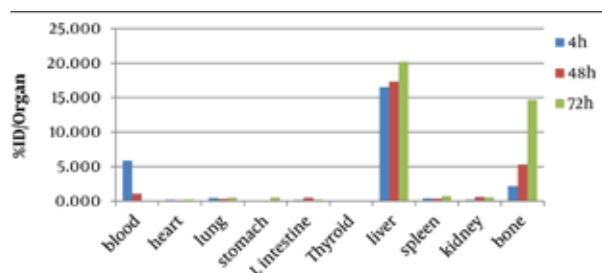
Figure3: Extrapolation of rat %ID/g to human %ID/organ for ^{46}ScCl$_3$
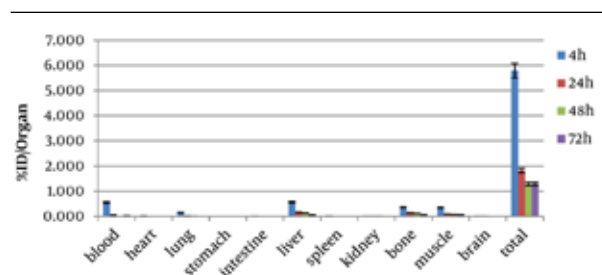
Figure4: Extrapolation of rat %ID/g to human %ID/organ for ^{46}Sc-BLM

Conclusion: In the present study, 46Sc–bleomycin complex was prepared with high radiochemical purities (>98%) under the optimized conditions. The proposed radiolabeled complex exhibited excellent stability at room temperature. The radiochemical purity of the sample was checked by ITLC (>99% using 2 solvent systems). At optimized conditions, total labeling and formulation of 46Sc-BLM took about 24 hours, with a radiochemical yield higher than %98. The radiolabeled complex was stable in aqueous solutions for at least 48 hours and no significant amount of

other radioactive species was detected by ITLC. The biodistribution of labeled compound was checked in mice up to 3 days and a significant accumulation took place in liver, bone, spleen, and kidneys that was in accordance with those of other reported radiolabeled bleomycin compounds. The absorbed dose in human was estimated by extrapolation of biokinetic algorithm in mice. In a study by Kairemo et al., the dosimetry in patients was 19 mGy in liver, 75 mGy in kidney, and 1.0 mGy in whole body (5 hours mean residence time) by the injection of 85 MBq and 100 MBq/mgIn-111-A′2a−c-BLMC. E.D.Williams estimated the absorbed dose from an injection of 1 mCi of 111In-bleomycin to the whole body as 0.3 rad, and approximately 1 rad to bone marrow, kidneys, liver, and spleen. In the present research, the absorbed dose of 100MBq injection to whole body was estimated to 0.72 mGy (3.563 hours mean residence time), and 0.86, 0.84, 1.53, and 0.92 mGy to red marrow, kidneys, liver, and spleen, respectively. Decay characteristics of ^{47}Sc were potentially useful for radionuclide tumor therapy, similar to those of the clinically established-^{177}Lu ($T_{1/2}$, 6.65 d; Eβav, 134 keV; Eγ, 113, 208 keV). The most obvious difference between ^{47}Sc and ^{177}Lu was the significantly shorter half-life of ^{47}Sc.

The comparison of the obtained data showed the lower absorbed dose to critical organs such as liver, kidney, spleen, and also bone marrow.

These results showed that^{47}Sc-BLM is a potential therapeutic compound and the current study experiments on this compound showed satisfactory quality, stability, and lower required dose, suitability for future therapeutic studies.

Keywords: Bleomycin; Scandium-47; Biodistribution; Dosimetry

Table3: Estimated Absorbed Dose and Residence Time for Human Organs

Target Organ	Dose (mGy/100MBq)		Residence Time τ(h)	
	^{47}Sc-BLM	^{47}ScCl$_3$	^{47}Sc-BLM	^{47}ScCl$_3$
Lung	0.4040	0.6117	0.0353	0.02834
Stomach	0.3566	1.8060	0.0052	0.013041
S-intestine	0.2620	1.6167	0.0062	0.033971
L-intestine	0.8683	5.1289	0.0062	0.34998
Liver	1.4514	4.5987	0.2133	0.545371
Spleen	0.6235	2.8628	0.0069	0.024359
Kidney	0.3358	3.1141	0.0023	0.047795
Bone	0.7522	4.0704	0.1494	0.750341
Red marrow	0.4528	2.5827	0.02	0.09094
Whole body	0.3221	1.7935	1.37	8.5787

■ The Correlation Between the Dose of a Calculation Reference Point and Planning Volume Mean Dose in Three-dimensional Conformal Radiotherapy of the Breast Using the Single-isocenter Half-beam Technique

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Abstract

Introduction: In 3-dimensional radiotherapy (3DCRT) of the breast or chest wall, the planning treatment volume (PTV) is used together with supraclavicular fossa by the single-isocenter half-beam (SIHB) technique of treatment planning. The half-blocked beams are matched using a single-isocenter to facilitate the SIHB technique.

However, since in the SIHB treatment plans the junction of separate fields suffers from great dose inhomogeneities as well as steep dose gradients, a potentially more serious problem with the SIHB technique is that the isocenter does not satisfy the requirements of the ICRU (International Commission on Radiation Units) point for dose prescription. Therefore, the dose calculation point should be selected in an off axis point.

In the present study, 2 dose calculation reference points were proposed for treatment planning of the breast cancer patients treated with the SIHB technique.

Materials and Methods: A total of 89 patients with breast cancer were selected for this study. The treatment planning of each patient was performed using the SIHB technique. Two PTV sites including supraclavicular region (PTV-1) and tangential region (PTV-2) were countered. Then, half-blocked beams were used to match the adjacent fields. The appropriate wedge angles and beam weights were chosen to improve the homogeneity of the dose distribution.

The reference calculation points at 3-dimensional rectangular coordinate system, the SRPs, were introduced by triple coordinates of x, y, and z. The coordinates indicated the signed distance along the coordinate axes, the x-axis (transverse distance), y-axis (axial distance), and z-axis (vertical distance or depth). In order to determine the SRPs, the point firstly was placed at the depth of 3-3.5 cm of the PTV-1 (Z), depending on the patient thickness, for the supraclavicle field. Then, at the same computed tomography (CT) slice, the Y and X coordinates were determined. The SRP was closely located on the clavicle (X), while one-third of the longitudinal length was under the superior edge of the field (Y). The reference calculation point for PTV-2 site of the breast was located on the anterior of chest wall (Z), at the middle of longitudinal length (Y).

Treatment plans were delivered with 6 MV X-rays and the Elekta was equipped with 40 pairs of multi-leaf collimator (MLC). All dose calculations were made by the collapsed-cone algorithm. The treatment planning system (TPS) used in the study was the Isogray (Dosisoft, Cachan, France). The prescribed dose for each PTV was 50 Gy in 25 fractions at 2 Gy per fraction.

The dose homogeneity index (DHI) was used for evaluating the target dose homogeneity. Furthermore, the dose–volume histogram (DVH) was obtained for each individual plan. Then, volume and dose (PTV, PTV mean and median) information was extracted from the DVHs. Next, doses at the suggested reference points (SRPs) (D_{SRPs}) were compared with the PTV mean (D_{mean}) and median (D_{median}) doses (the paired t test).

Results: The dose homogeneity in all treatment plans was almost perfect (DHI= 0.07 and 0.09 in PTV-1 and PTV-2, respectively). In 75% of the cases, the differences between the doses in the SRPs (D_{SRPs}) and D_{mean} to the PTVs were less than 3%, in 33% of the cases were less than 2%, and in 13% of the cases were less than 1%. The D_{SRPs} were equal to D_{median} in both the PTVs (P >0.05). The difference between the SRP and PTV mean/median doses was not affected by the size of the PTVs (P >0.05).

Conclusions: Results of the study showed that the doses in the

ABSTRACT

D_{SRPs} in patients with breast cancer can be accurately assessed by D_{mean}/D_{median} of the adjacent treatment sites. Accordingly, the proposed points satisfied the recommendations of the ICRU reference point and therefore, were clinically relevant. Furthermore, the D_{SRPs} are the representative of the dose throughout the 2 PTV sites. Similarly-configured prescription reference point could lead to a more certainty in the prediction of radiation response as well as the intercomparison of different centers to establish consistent treatment planning methods.

Keywords: Prescription Dose; Single-isocenter half-beam Technique; ICRU Reference Point; Mean Dose; Median Dose; Field Matching

INDEX

INDEX

INDEX

Reports of Radiotherapy & Oncology