



6th International TPCF Preclinical Imaging Symposium



The Pivotal Role of Preclinical Imaging in Translational Medicine

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Editorial

As we step into 2023, the landscape of translational medicine continues to evolve, revealing the profound importance of preclinical imaging in bridging the gap between laboratory discoveries and clinical applications. Preclinical imaging allows researchers to visualize biological processes in real time, providing invaluable insights into the efficacy and safety of new therapeutic strategies.

The ability to monitor changes at the organ, tissue, cellular, and molecular levels is not just a technological feat; it is a cornerstone of modern biomedical research. Non-invasive imaging techniques, such as high-frequency micro-ultrasound, MRI, CT, and advanced molecular imaging modalities like PET and SPECT, empower scientists to track disease progression and treatment responses longitudinally. This capability is particularly crucial in translational medicine, where understanding the dynamics of disease and therapy can lead to more effective interventions.

At the forefront of this innovation is the TPCF (Tehran University of Medical Science Preclinical Core Facility), which champions the integration of science and technology in preclinical imaging. The 6th International TPCF Preclinical Imaging Symposium (TPIS 2023) promised to be a pivotal event for researchers dedicated to enhancing translational research. With an impressive lineup of keynote speakers and workshops, the symposium delved into cutting-edge imaging technologies that are revolutionizing drug discovery and development.

The significance of preclinical imaging cannot be overstated; it not only accelerates the translation of research findings into clinical settings but also fosters collaboration among scientists, engineers, and clinicians. By sharing knowledge and resources, we can collectively push the boundaries of what is possible in medical science.

We are excited that Frontiers in Biomedical Technology (FBT) will once again publish the abstracts from the TPIS 2023, ensuring that groundbreaking research reaches a wider audience. We invite all interested researchers and professionals to join us at TPIS 2024 for an enriching experience that promises to inspire new ideas and partnerships.

For more information about the symposium and registration details, please visit our website at www.TPCF.ir. Together, let us continue to illuminate the path from bench to bedside through the transformative power of preclinical imaging.



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Effects and Efficiency of HIFU on Treatment of Cancer and Biological Abnormalities

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Abstract

Background: Considering the importance of minimal side effects and maximum efficiency of a treatment procedure, HIFU (High Intensity Focused Ultrasound) has been used as a relatively new and minimally invasive method for many tumors and abnormalities. The present study was conducted to investigate the effects of HIFU on tumor and the treatment efficiency of abnormalities in biological tissues in preclinical studies.

Materials and Methods: The databases of PubMed, science direct, Web of Science and Google scholar were explored. Using the following key words: High Intensity Focused Ultrasound (HIFU), HIFU AND cancer, HIFU AND cancer treatment, HIFU AND Rat, HIFU AND mice, HIFU AND Rabbit. The obtained results were screened for the Title and abstract by two authors and the relevant papers were reviewed for further details.

Results: 14 studies were investigated in this research. 7 of the reviewed studies (50%) were related to Rat, 3 cases (21.43%) were related to Rabbit and 4 cases (28.57%) were related to mice. Most of the investigated tumors included liver, brain and colon. Some of them studied the effect of HIFU on viral diseases and the reaction of the immune system to these diseases following the use of HIFU. The effects of HIFU on the tumor included coagulation necrosis in the tumor and necrosis due to decreased blood flow. Moreover, related studies observed effects such as reducing tumor growth, volume and size, apoptosis induction, and further tumor suppression, when used HIFU concurrently with chemotherapy or surgery. Furthermore, HIFU can reduce the Intravascular Growth Factor (IGF) in certain types of tumors. Longevity has also reported for most HIFU-treated study samples. Improving the transfer and distribution of chemotherapy medicines in all parts of the tumor, destroying the blood-brain barrier of the tumor, inducing sensitivity in the immune system and improving the effectiveness of the tumor ablation compared to other treatment procedures, reducing the duration and increasing the peak tumor uptake rate of radiolabeled monoclonal antibodies have also stated in reviewed studies. By affecting the immune system, HIFU helps to improve the efficiency and prolong the effect of vaccines used for viral diseases. Thrombotic effects and destruction of the arterial membrane have also been reported. It should be noted that all the mentioned effects depended on HIFU intensity and tissue characteristics. So that the best results were obtained when the frequency was 2.5 MHz and the exposure was 4300 W/cm².

Conclusion: In general, the results of the reviewed studies indicated that HIFU has a direct effect on reducing tumor growth and volume and improves the effect of other methods of tumor inhibition such as chemotherapy and surgery. Also, improves the efficiency of the immune system. Future studies are required for another kinds of cancers and abnormalities for widening information about HIFU efficiency.

Keywords: High Intensity Focused Ultrasound; Efficiency; Cancer; Abnormality.



6th International TPCF Preclinical Imaging Symposium



Beyond the One-Size-Fits-All Approach: The Role of Imaging Biomarkers and Genomics in Precision Oncology: A Comprehensive Review

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Abstract

Background: Precision medicine is a medical approach that aims to offer “tailored” diagnosis and treatment by analyzing individual patients' genetic characteristics. In recent years precision medicine had substantial advances in the field of oncology and cancer management via the employment of genomics. Genomics is an emerging medical field that investigates the cancer cell DNA and thus plays an important role in cancer research by identifying mutations that lead to cancer. In addition to genomics, imaging biomarkers are also employed in cancer research to detect abnormalities and accelerate the treatment responses to cancer. Imaging biomarkers are objective biological features that provide solid information about the tumor's characteristics. Integrating imaging biomarkers with genomics in conjunction with a precision medicine approach enhances our understanding of cancer biology and aids in more effective treatment responses for patients with cancer.

This paper aims to explore the role of Precision Medicine in Oncology, focusing on identifying the important biomarkers for diagnosis, prognosis, and treatment of cancer.

Materials and Methods: We performed an extensive search with the following keywords: “Precision Medicine” “Imaging Biomarkers” “Genomics” and “Cancer” in Google Scholar and PubMed databases. The related articles were included based on their relevance to the main topic of the search. Most of the articles were excluded for not meeting the inclusion criteria relating to precision medicine approaches, imaging biomarkers, and genomics for cancer diagnosis and treatment. In our review, we focused on the evaluation of various imaging biomarkers associated with genomics in specific types of cancer.

Results: Our search strategy resulted in approximately 16,900 articles. After screening the titles and abstracts, we assessed 143 full-text articles for eligibility. Of those, 100 articles were excluded for the following reasons: 31 articles did not specifically discuss the use of imaging biomarkers. 43 articles did not focus on genomics in relation to imaging biomarkers. 26 articles were review articles, editorials, or case studies. A total of 43 relevant articles were finally included in this review. Some of the key imaging biomarkers assessed include KRAS, PTEN, PAM50, PSMA, and HER2. For instance, mutations in KRAS genes indicated the advancement of lung cancer. The results of studies suggest that change, loss, or mutations in some specific genes can correlate directly to the progression of different types of cancer.

Conclusion: Imaging biomarkers play an important role in realizing the promise of precision oncology. They provide quantifiable features that can aid in cancer diagnosis, prognosis, and treatment monitoring. When integrated with genomic data, imaging biomarkers can reveal genomic mechanisms driving tumor development and identify targets for tailored therapies. However, there are challenges that still need to be addressed, such as costs and limited expertise. If these obstacles can be overcome precision medicine has the potential to greatly enhance cancer management in healthcare settings. Through refinement and progress, we may soon witness the impact of precision medicine on improving outcomes for cancer patients and their quality of life.

Keywords: Cancer; Precision Medicine; Imaging Biomarkers; Oncology.



6th International TPCF Preclinical Imaging Symposium



Efficiency and Application of Artificial Intelligence in Preclinical Procedures

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Abstract

Background: Artificial intelligence raised as a new and practical method in medical sciences. Various studies have been conducted regarding its use in imaging, as a complementary method in the diagnosis and treatment of cancer and other diseases.

The aim of the present study was to review the efficiency and application of artificial intelligence in preclinical researches.

Materials and Methods: The databases of PubMed, Science Direct, Web of Science and Google Scholar were explored. Using the key words: Artificial Intelligence (AI) AND rat, artificial intelligence AND mice, artificial intelligence AND rabbit, artificial intelligence AND preclinical. The results obtained for the title and abstract were studied by authors and the relevant articles were reviewed for more details.

Results: Using deep learning algorithms in medical and biological fields has brought significant findings. Assessment of hepatocellular hypertrophy using artificial intelligence showed that this procedure can be helpful in detecting cytoplasmic levels, especially in central lobular areas. Correlation with histopathological grading was also observed. Artificial intelligence indicated potential in helping to diagnose cardiomyopathy and improve the accuracy of tumor detection in medical images. Furthermore, AI-based image analysis has a strong correlation with manual counting to evaluate proliferation in reproductive tissues. In forensic science, AI can estimate time to death, while in chemistry-related explainable AI (XAI), it provides an integrated gradient framework for Absorption, Distribution, Metabolism, and Excretion (ADME).

Conclusion: Artificial intelligence has significant potential in simplifying, increasing accuracy and efficiency of medical and biological researches from liver cell hypertrophy to cardiomyopathy diagnosis, tumor diagnosis, and forensic investigations. Its continued development promises transformative advances in healthcare, biology and chemistry applications that benefit both researchers and patients.

Keywords: Efficiency; Artificial Intelligence; Preclinical.



6th International TPCF Preclinical Imaging Symposium



Observation of Morphological Alteration of Breast Cancer Cells (MCF7) after X-Ray Irradiation Based on Digital Holographic Microscopy (DHM)

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Abstract

Background: Radiotherapy, one of the primary methods for cancer treatment, utilizes X-rays to target tumor tissue. However, radiation affects all exposed tissues, resulting in various changes, including morphological alterations in cells. Understanding these changes and their phenotypic patterns is crucial in multiple fields, including predicting cellular response to treatment. This study aims to explore the potential of digital holographic microscopy in assessing the visual changes in irradiated cells.

Materials and Methods: MCF7 cells were exposed to a single fraction of radiation, with a dose of 2 Gy in the radiation group. Morphological changes in the irradiated cells and the control group were evaluated using digital holographic microscopy. The acquired images were reconstructed and analyzed using MATLAB software. The morphological changes of MCF7 cells were investigated based on parameters such as volume, Standard Deviation (STD), kurtosis, and skewness.

Results: Microscopic measurements revealed morphological changes in the irradiated cells through image analysis. The results demonstrated significant differences in volume, kurtosis, and skewness between the irradiated cells and the control group.

Conclusion: Holographic microscopy, as a label-free and non-invasive technique, effectively captures the morphological changes in living cells. By extracting various parameters and expanding the range of morphological and physical parameters, it becomes possible to establish a more accurate correlation between cellular conditions and treatment response.

Keywords: Digital Holography Microscopy; Morphological Changes; Radiation; MCF7 Cells.



Evaluation of Liver Tissue Stiffness in Non-Alcoholic Fatty Liver Disease Using the Imaging Technique of Acoustics Radiation Force Impulse (ARFI)

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Abstract

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease. The spectrum of NAFLD varies from simple steatosis (Non-alcoholic fatty liver) to non-alcoholic steatohepatitis. Liver biopsy is the gold standard method to quantify hepatic steatosis. Due to its invasive nature, non-invasive imaging methods are evolving to replace biopsy. Conventional ultrasonography provides relatively good accuracy for the qualitative diagnosis of moderate to severe hepatic steatosis but has limited accuracy for mild steatosis. In liver steatosis, the flexibility of the liver tissue is reduced, so it is essential to extract the stiffness of the liver tissue. In this study, the ability to quantitatively diagnose healthy and steatosis liver tissue from the acoustic radiation force impulse elastography technique. It is investigated by two methods: point Shear Wave (p-SWE) and Two-Dimensional Shear Wave (2D-SWE).

Materials and Methods: 27 individuals (9 men and 18 women, 20-50 years), without any underlying liver disease, were examined. Evaluation with an ultrasound device equipped with a curved array probe (1-7 MHz) qualitatively confirmed 15 individuals with healthy liver and 12 patients with fatty liver. These people were subjected to liver stiffness measurement using two p-SWE and 2D-SWE methods. Finally, the tissue stiffness of healthy and fatty livers was quantitatively extracted. An independent t-test with a significant level of 0.95 ($p < 0.05$) was used to determine the difference between the two groups. Point shear wave elastography (P-SWE) without displaying the color image and two-dimensional shear wave elastography estimated liver stiffness over a larger area with a color-coded elastogram.

Results: The results showed that the mean liver tissue stiffness by the point shear wave method in patients with fatty liver is 4.33 ± 1.02 kPa significantly increased compared to healthy liver with a stiffness of 3.55 ± 0.91 kPa (22%) ($P < 0.05$). The quantity of liver tissue stiffness by the two-dimensional shear wave method in patients with fatty liver was 5.03 ± 1.44 kPa compared to healthy individuals with a stiffness of 4.57 ± 1.14 kPa, which did not show a significant difference ($P > 0.05$).

Conclusion: These findings show that in the elastography- mode of ultrasound imaging, the point shear wave technique can differentiate fatty liver tissue stiffness from healthy liver relative to the two-dimensional shear wave method.

Keywords: Ultrasound Imaging; Non-Alcoholic Fatty Liver; Elastography; Stiffness.



6th International TPCF Preclinical Imaging Symposium



Terahertz Computed Tomography and Imaging Challenges

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Abstract

Background: Terahertz (THz) imaging has emerged as a promising technique for non-destructive evaluation and imaging applications, offering unique advantages over traditional imaging modalities. This paper presents an overview of the current state of Terahertz Computed Tomography (THz-CT) and highlights the challenges faced in its implementation. THz-CT utilizes electromagnetic waves in the terahertz frequency range to reconstruct three-dimensional images of objects with high resolution and penetration capabilities. The ability to visualize internal structures without the use of ionizing radiation has significant implications for various fields, including medicine, security, and material science.

Materials and Methods: Despite its potential, THz-CT faces several challenges that need to be addressed for its widespread adoption. Firstly, the limited availability and complexity of THz sources and detectors hinder the practical implementation of THz-CT systems. Efforts are being made to develop compact, efficient, and cost-effective THz sources and detectors to overcome these limitations. Secondly, THz waves are highly susceptible to scattering and absorption by various materials, including water and certain organic compounds. This poses challenges in achieving accurate and artifact-free reconstructions, especially in applications involving biological samples. Researchers are exploring advanced signal processing techniques and novel imaging algorithms to mitigate these effects and enhance image quality.

Results: Furthermore, the relatively long acquisition times required for THz-CT imaging limit its real-time applications. Efforts are underway to develop faster acquisition methods, such as multi-view imaging and compressed sensing, to reduce acquisition times while maintaining image quality. Lastly, the lack of standardized protocols and benchmarks for THz-CT imaging hinders the comparison and reproducibility of results across different systems and studies. Establishing common evaluation metrics and guidelines will facilitate the development and validation of THz-CT techniques. Also, in addition to its various applications, terahertz medical imaging plays a significant role in the diagnosis of several types of cancers, including skin, oral, breast, and colon cancers. One of the key advantages of terahertz radiation is its exceptional sensitivity to water content, enabling the creation of high-contrast images that effectively differentiate between normal and cancerous tissues. This capability proves instrumental in accurately identifying and assessing the presence of cancer in affected areas.

Conclusion: In conclusion, Terahertz Computed Tomography holds great promise for various imaging applications, but several challenges need to be overcome for its widespread adoption. Addressing the limitations associated with THz sources, scattering and absorption effects, acquisition times, and standardization will pave the way for the realization of the full potential of THz-CT in the future.

Keywords: Terahertz Imaging; Computed Tomography; Terahertz Computed Tomography; Challenges; Terahertz Sources; Scattering; Absorption; Acquisition Times; Standardization.



Using a New 2D Matrix Based Neural Network to Accurate Automatic Segmentation of Volumetric SPECT Data

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Abstract

Background: Quantifying the Left Ventricle (LV) in nuclear medicine images poses a challenge for myocardial perfusion scintigraphy. In this study, we developed and tested a hybrid method for automated left ventricle myocardial border extraction in Single Photon Emission Computed Tomography (SPECT) datasets, aiming to automate LV ventriculography.

To achieve automatic segmentation of the LV in volumetric SPECT data, we implemented hybrid techniques consisting of a novel 2D matrix-based neural network and a variational level set algorithm. The method involves three main steps: initialization, feature extraction and primary contour estimation using the level set algorithm, and segmentation. Initially, we estimate the initial closed curves in SPECT images using adaptive thresholding and morphological operations. Subsequently, we utilize these initial closed curves to estimate the contour using the variational level set algorithm, and finally, we employ them as input to the neural network.

Materials and Methods: To evaluate the performance of our proposed approach, we compared the manually obtained boundaries with the automated segmentation contours in 10 SPECT datasets obtained from adult patients. We visually compared the segmented images generated by the proposed method with manually outlined contours and assessed the performance using ROC analysis.

Results: We compared the proposed method with traditional methods by computing the sensitivity and specificity of ventricular outlines, as well as conducting ROC analysis. The results demonstrate that the proposed method effectively segments LV regions with a sensitivity and specificity of 88.1% and 95.2%, respectively. The experimental results highlight the effectiveness and reasonable robustness of the automatic method.

Conclusion: In conclusion, our study introduces a new hybrid technique capable of automatically tracing the LV contour in cardiac SPECT datasets, leveraging the characteristics of the overall region of LV images. This method achieves smooth and accurate LV contours by utilizing the new neural network reconstruction and considering the influence of neighboring correlation in the image matrix.

Keywords: Cardiac Single Photon Emission Computed Tomography; Matrix Based Neural Network; Left Ventricle Segmentation; Myocardial Perfusion Scintigraphy.



6th International TPCF Preclinical Imaging Symposium



Evaluation of Homing and Migration of Activated Natural Killer Cells which Injected from Different Roots in Xenograft Model of Hepatocellular Carcinoma Via Ex Vivo Imaging

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Abstract

Background: Ex vivo-expanded Natural Killer (NK)-cell-based immunotherapy is emerging as an attractive approach for cancer treatment. However, to development of effective clinical implementation, the migration and functionality of activated NK cells toward solid tumors is the important questions which must be answered. Therefore, the non-invasive tracking of adoptive NK cells plays a crucial role in post-treatment monitoring and also in offering opportunities for preclinical studies.

Tracking administered Natural Killer (NK) cells in vivo is critical for facilitate and expedite clinical implementation of NK cells for treatment of human Hepatocellular Carcinoma (HCC). Here the ex vivo-imaging of activated Green Fluorescent Protein (GFP) labeled NK cells was investigated for tracking the distribution of adoptive NK cells during HCC progression.

Materials and Methods: Ex-vivo NK cells were isolated from healthy donors and were activated and labeled with a fluorescent dye (GFP). The proliferation, surface receptor expression and cytotoxicity activity of NK cells were evaluated in different injection methods. For implantation of xenograft HCC tumors, the human HepG2 cells were injected bilaterally into the subcutaneous region of two flanks of nude mice. Then the animals were randomly divided into three groups: the first group received (GFP)-labeled NK cells systemically, the second received intra-tumoral GFP-labeled NK cells and the third received PBS. After 40 days of tumor cell injection, the animals were scarified and after measuring the tumor volumes, some part of tumors transferred to formalin buffer for H&E staining and immunohistochemistry analysis (KI67), and the others were used for ex-vivo imaging. Blood samples were taken from all subjects before sacrificing them. Single cell suspensions from the resected organs were analyzed using flow cytometry.

Results: Ex-vivo imaging illustrated homing of more GFP labeled NK- cells in tumor tissues derived from the group receiving intra-tumoral NK-GFP compared to systemically injected group. In the xenograft HCC tumors, the NK cell fluorescence signal was the highest in the liver for 7 days after NK injection and persisted for 14 days. The purity of persistent CD56+CD3- NK cells in HepG2-bearing mouse was very higher than control group. In addition, Ki-67 expression level of HCC tumors significantly reduced in the intra-tumoral injected NK cells group compared to other groups.

Conclusion: Administered NK cells were successfully tracked in vivo by labeling the NK cells with GFP. The intra tumoral injected NK cells showed the better homing, functionality and cytotoxic activity against HCC tumors. So, the local injection of activated NK cells could be a better root administration than systemic injection.

Keywords: Hepatocellular Carcinoma; Natural Killer Cells; Ex-Vivo Imaging; Local or Systemic Injection.



6th International TPCF Preclinical Imaging Symposium



Radiographic Evaluation of Medial Patellar Luxation in Pomeranian Dogs by Measuring Quadriceps Angle (Q Angle) and Femoral Varus Angle (FVA)

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Abstract

Background: Patellar luxation is one of the common diseases in small breed dogs, especially Pomeranian dogs. This disease causes pain and lameness of hind-limbs the affected animal. Accurate diagnosis of this disease is of great importance in order to effectively intervene in it. Radiography is one of the simple yet accurate tools that help for evaluating and grading of this disease.

The purpose of this study was to identify the size of the Quadriceps Angle (Q angle) and Femoral Varus Angle (FVA) in Pomeranian dogs with different grades of Medial Patellar Luxation (MPL).

Materials and Methods: This study was conducted on Pomeranian dogs, whose MPL was clinically confirmed, and Putnam (1968) classification was used in its conduct. Each MPL, grade 1, grade 2, grade 3 and grade 4, 4 hind-limb from 11 Pomeranian dog were considered and two angles Q and FVA were measured in them. The Q angle is the result of the intersection of two lines, one of which connects the center of the patella bone to the tibial tuberosity and the other line that connects the anterior cruciate ligament to the center of the patella bone (Kaiser *et al.*, 1997). The FVA angle is also the result of the intersection of two lines, one connecting the center of the patella to the proximal center of the femur, and the other one that connecting the center of the patella to the center of the tibia (Hauptman *et al.*, 1985). In the process of studying the angles were measured and the average of each parameter was recorded separately for samples.

Results: The results of this study showed that the mean Q angle in dogs with I, II, III and IV patellar luxation is 11, 16, 22 and 36 degrees, respectively. It was also found that the difference between the mean Q angle in different grades of luxation is statistically significant. The mean of FVA angle in dogs with I, II, III and IV patellar luxation were 28, 23, 22 and 16 degrees, respectively, These means were not statistically significantly different from each other.

Conclusion: According to the findings of this study, measuring the Q angle and FVA angle can be helpful in prognosis of disease and degree of progressivity of luxation situation and changing the grade of disease in patient and making an acceptable decision for conservative or surgical treatments.

Keywords: Quadriceps Angle; Medial Patellar Luxation; Radiography; Pomeranian.



6th International TPCF Preclinical Imaging Symposium



Performance Improvement of Breast Imaging Systems

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Abstract

Background: The Scattered radiation is the principal factor affecting the quality of the mammography images. The Contrast Improvement Factor (CIF) and Bucky Factor (BF) parameters, respectively referred to as the benefit and cost of the anti-scattered grid, cannot be appropriately assessed without detailed knowledge of the scattered radiation.

The main goal of this study is to design a two-dimensional anti-scatter grid to impose the patient dose to a minimum level and improve the image quality simultaneously.

Materials and Methods: A comprehensive 3D Monte Carlo simulation of two-dimensional anti-scatter grid parameters has been performed to optimize the performance of breast imaging systems. A combination of IEC 60627:2013 international standard exposure condition, perfect energy integrating detector model, and more clinical parameters were considered for this simulation.

Results: The performance of more than 450 different two-dimensional anti-scatter grid has been investigated. A wide range of calculations were performed so that grid ratio r , strip density N , strip thickness d values respectively were $r=2-14$, $N=10-100$ (1/cm), and $d=4-30$ μm . The optimized grid in this work has $\text{BF}=2.17$, $\text{CIF}=1.44$, strip thickness of 30 μm and strip density of 10 1/cm and grid ratio of 4.

Conclusion: Based on the obtained results this grid has produced the least dose to the patient compatible with the concept of ALARA, and the maximum improvement on the image contrast.

Keywords: Mammography; Monte Carlo; Optimization; Two-Dimensional Anti-Scatter Grid.



Reliable Segmentation of Glioblastoma Multiforme Using Quantitative Susceptibility Mapping: Case Report

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Abstract

Background: Glioblastoma Multiforme (GBM) is the most common and malignant primary tumor of the brain with a high recurrence rate and poor diagnosis. Magnetic Resonance Imaging (MRI) using gadolinium-based Contrast Enhancement (CE) is the common method of choice for the evaluation of GBM. However, this method has a poor indication of volumes of metabolically active tumors, leading to necrosis area enhancement (false positive) in some cases, which would be entirely a random phenomenon. Gadolinium-enhancing necrosis could be mistaken for an active tumor, creating difficulty for the auto-segmentation of GBM. Therefore, the development of imaging methods to detect metabolically active areas of the tumor with high reliability is very worth to be addressed.

This case report study aimed to demonstrate the potential of state-of-the-art susceptibility-based MRI using a new contrast agent “5-Aminolevulinic Acid (ALA) plus iron supplements” for discriminating the necrosis and metabolically active parts of the GBM in the case of gadolinium-enhancing necrosis.

Materials and Methods: In this study, following administration of ALA and ferric ammonium citrate (FAC, 6 h after ALA, intra-tumoral injection) to animals, all animals (six rats) were randomized to the “ALA+FAC” group, imaged using MRI. Briefly, the anesthetized rats were positioned parallel to the magnetic field. Then, the brain of rats imaged axially with a 3 T MRI scanner using a flow-compensated, 3D multi-echo GRE sequence for T2* and Quantitative Susceptibility Mapping (QSM), and T1-weighted Turbo Spin Echo (TSE) sequence for CE after administration of dotarem. Then, the acquired images were analyzed and compared statistically.

Results: Among six rats, an enhancement was observed in the necrosis area of the GBM of a case, representing a gadolinium-enhancing necrosis which is entirely a random phenomenon. While the Signal Intensity (SI) of the active and necrosis areas of the case in the CE image demonstrated no significant difference, the SI on the T2*-weighted images and susceptibility values in QSM changed 24 and 150%, respectively.

Conclusion: These results provide valuable insights into the potential of susceptibility-based MRI using ALA+FAC to apply as a robust discriminator between necrotic and viable tumors.

Keywords: Glioblastoma Multiforme; Active Metabolically Contours; 5-Aminolevulinic Acid; Quantitative Susceptibility Mapping.



6th International TPCF Preclinical Imaging Symposium



CT Anatomy of The Mandible and Hyoid Apparatus in The Alborz Wild Sheep

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Abstract

Background: The Central Alborz wild sheep is a hybrid of the Urial ram with 58 chromosomes and the Armenian ram with 54 chromosomes. This ram is one of the largest hybrids mentioned. Computed Tomography (CT) scan is one of the non-invasive techniques that uses X-ray beam to give a sectional view of the body without superimpositioning of adjacent organs. In head CT scan, useful information is obtained by providing accurate cross-sectional images of the nasal cavity, paranasal sinuses and brain cavity.

Understanding the anatomical structures of endangered wildlife species is a real help for veterinarians in this field. The aim of this study was to determine the anatomy of the skull of this sheep, which is phenotypically similar to deer.

Materials and Methods: In this study, the skulls of 6 male Alborz wild sheep, all alive, were examined. The examinations were performed using CT scans and radiographic images. It also processed and named the extracted images using RadiAnt and Photoshop software.

Results: Morphometric examinations of the mandible showed that the bone was 18.55 ± 0.48 cm long on average. Also the average height of this bone from the lowest part to coronoid process was calculated to be 10.58 ± 0.52 cm. The average distance between the last inciseive tooth to the mental foramen (MFID) and the first pre-molar tooth to the mental foramen (MFPD) were calculated as 2.03 ± 0.60 and 2.52 ± 0.66 cm, respectively. The hyoid apparatus consists of 4 pairs of bones, the tallest and smallest of which are stylohyoid and epihyoid, are 5.66 ± 0.45 and 1.14 ± 0.47 cm long on average, respectively. Also, the average lengths of ceratoyoid and thyrohyoid were 1.54 ± 0.42 and 1.33 ± 0.44 cm, respectively.

Conclusion: The average size of the first inciseive tooth in Alborz wild sheep and Ile de France sheep were 0.67 ± 0.33 and 0.55 ± 0.01 cm, respectively. Also, the average length of the first pre-molar and molar tooth in Ile de France sheep was 0.78 ± 0.22 and 1.62 ± 0.12 cm, respectively. Morphometric results shows, all tooth of Alborz wild sheep are larger than Ile de France sheep. Considering that the Alborz wild sheep is one of the Iranian endangered breeds, knowing the anatomy of the head region is of particular importance.

Keywords: Computed Tomography Scan; Alborz Wild Sheep; Mandible; Hyoid Apparatus.



6th International TPCF Preclinical Imaging Symposium



Morphometric Study of The Skull of The Ile de France Sheep

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Abstract

Background: The Computed Tomography (CT) scan imaging technique provides a situation for Clinicians to give the fastest and best diagnosis of many diseases of the skull and body without causing changes in the body. The Ile de France has been bred in France since 1822. The first Ile de France sheep arrived in South Africa in 1903. Ile de France sheep is one of the meat-producing breeds and is especially popular among farmers due to its high twinning.

As far as we know morphometric information in the Ile de France sheep has not been previously reported. These data are very important to meet the demands of many surgeons and internal medicine veterinarians about the anatomy of the head in Ile de France sheep.

Materials and Methods: The total skull length, height and width were 25.3 ± 1.02 , 9.8 ± 0.93 , and 12.3 ± 0.91 cm, respectively. Incisor's teeth in this breed were only in the mandible and there were 4 in each half of the jaw and the average measured length was 0.58 ± 0.01 cm. The distance between auditory ossicles to external acoustic meatus was 2.16 ± 0.05 cm. Also, the distance between Temporo-Mandibular Joint (TMJ) and auditory ossicles was 2.1 ± 0.12 cm. There were molar and premolars in the upper and lower jaws and 3 premolars and 3 molar teeth were observed in each half of the jaw. However, in one of the male samples, the last molar tooth was not observed. The mandible in the ruminants has the space between the last incisor and the first pre-molar tooth, called interalveolar space or diastema. The average length of the interalveolar space was 3.8 ± 0.32 cm. The mean total skull length of the Ile de France sheep was found to be 25.3 ± 1.02 cm.

Results: The total skull length, height and width were 25.3 ± 1.02 , 9.8 ± 0.93 , and 12.3 ± 0.91 cm, respectively. Incisor's teeth in this breed were only in the mandible and there were 4 in each half of the jaw and the average measured length was 0.58 ± 0.01 cm. The distance between auditory ossicles to external acoustic meatus was 2.16 ± 0.05 cm. Also, the distance between TMJ and auditory ossicles was 2.1 ± 0.12 cm. There were molar and premolars in the upper and lower jaws and 3 premolars and 3 molar teeth were observed in each half of the jaw. However, in one of the male samples, the last molar tooth was not observed. The mandible in the ruminants has the space between the last incisor and the first pre-molar tooth, called interalveolar space or diastema. The average length of the interalveolar space was 3.8 ± 0.32 cm. The mean total skull length of the Ile de France sheep was found to be 25.3 ± 1.02 cm.

Conclusion: The skull length of Saanen goat reported 22.67 ± 0.93 cm, West African Dwarf goat 6.99 ± 1.59 cm, Markhor goat 18.67 ± 0.66 cm, and Alborz wild sheep 25.28 ± 0.99 cm. Also morphometric results shows that all bones of hyoid apparatus in Ile de France sheep are smaller than Alborz wild sheep. Considering the prominent role and high production capacity of this breed in the meat production industry, knowing the anatomical structures of the head area is of particular importance.

Keywords: Ile De France Sheep; Skull; Computed Tomography Scan; Morphometric Study.



Evaluating The Efficacy of Scaffolds Derived from Rice Plant for The Repair of Bone Defects in Preclinical and Future Clinical Studies

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Abstract

Background: Bone tissue engineering has been attracted as an alternative way to the conventional treatments particularly in large bone defects due to complex and arranged structure of bone components with inadequate regeneration capability. In this regard, exploiting bio-inspired multifunctional biomaterials has been suggested as promising and feasible resource attributed to their outstanding properties of availability, non-toxicity, biocompatibility, and biodegradability. Plant-derived cellulosic scaffolds possess numerous advantages to be used as therapeutics directly to the bone in order to achieve bone regeneration.

The present study aimed to investigate potential of using rice straw scaffold with different structures which contain silica in addition to cellulose on induction of osteocyte differentiation in human Bone Marrow-derived Mesenchymal Stromal Cells (hBMMSCs) and evaluate stem cells fate direction like adhesion, proliferation on these matrixes.

Materials and Methods: After decellularization of the rice straw and confirmation of removing plant cell materials, cellulosic scaffolds were assessed for their physical characteristics such as surface morphology, wettability, porosity and roughness using Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM) and X-ray Diffraction (XRD). Further, chemical properties of obtained matrices were found by means of Fourier-transform Infrared spectroscopy (FTIR). Consequently, osteogenesis induction potential of the scaffold for hBMMSCs cultured on them and culture plate as a control were compared by means of alizarin staining and calcium content, alkaline phosphatase activity assay as well as measuring bone marker genes expression ratios.

Results: The results of this research determined that rice straw scaffold do not have any toxicity for cells, and because of their favourable physicochemical properties, they are able to support stem cell adhesion, growth and proliferation. In addition, the rough grid nano-structure resulting from the presence of silica in the rice straw derived scaffold can lead to mechanical orientation needed to efficiently induce bone differentiation.

Conclusion: Data presented here highlighted the outstanding physicochemical, mechanical, and biological properties of rice straw scaffold to support the growth, proliferation and osteo-induction of hBMMSCs. In total, it can be concluded that nanostructure and silica content of scaffolds derived from rice straw, made it an ideal candidate for future bone tissue engineering clinical applications.

Keywords: Bone Defects; Regenerative Medicine; Tissue Engineering; Plant Scaffolds; Rice Straw.



Enhanced Bone Assembly on a Surface Functionalized Cannabis Leaves Derived Scaffolds

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Abstract

Background: Finding feasible and potent matrixes suitable for the scale-up and subsequent clinical commercialization of tissue engineered cell products mainly in bone regeneration is still challenging issue. In our previous attempts, we reported a sustainable approach for make herbal derived biocompatible and biodegradable scaffold capable of stem cell growth and differentiation. In this regard, developing a feasible scaffold with nano-structured surface able to replicate the structural properties of bone tissue's Extracellular Matrix (ECM) is necessary for clinical applications.

The purpose of this study is to evaluate potential of the functionalized cellulosic scaffold derived from cannabis leaves for induction of osteogenesis in adipose-derived human mesenchymal stem cells. As well as finding the relation between the surface modification of the scaffold on direction of the cell fate, and induction of osteogenic differentiation in Human Mesenchymal Stem Cells (hMSCs).

Materials and Methods: Various approaches were used to obtain best way for acellularization of the cannabis leaves as well as their surface modification. Consequently, physicochemical properties of the sole and surface modified scaffolds including such as hydrophilicity, porosity, surface roughness, mechanical properties, and specific surface area were evaluated using Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Fourier-transform Infrared Spectroscopy (FTIR) and X-ray Diffraction (XRD). Moreover, capability of obtained scaffolds to support cell viability, proliferation, adhesion, as well as induction of osteogenic differentiation in hMSCs were assessed followed by the investigation of the relative expression ratio of osteogenic markers using real time PCR, and Alkaline Phosphatase activity (ALP) assay.

Results: The porous and nanostructured hydrophilic structure of the scaffold, as evidenced by SEM and AFM analyses, exposed potency of cannabis-derived scaffolds in cell attachment and growth. Moreover, the biodegradable scaffold continued to degrade over time. Osteoinductivity of the scaffolds determined by the increased cell's ALP activity and mineralization confirmed that there are proper candidates for bone differentiation compared to the cultured cells on culture plate. In addition, the higher expression ratio of osteogenic markers such as Runx2, ALP, collagen-1 (Col-I), and osteocalcin showed promotive effects of scaffold in osteogenic differentiation of human hMSCs.

Conclusion: Data presented here revealed that scaffolds derived from cannabis leaves have favourable physicochemical properties for bone regeneration that would be enhanced by further surface modification and obtained matrixes are proper bioinspired scaffold for bone tissue engineering. Further preclinical analysis is needed prior to use such scaffolds in the clinics.

Keywords: Regenerative Medicine; Bone Tissue Engineering; Cannabis; Surface Modification.



Complete Title: Polyphenolic Bioactive Compounds Ameliorated the Cardiotoxicity in Gastric Cancer Mice Received Paclitaxel

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Abstract

Background: Cardiotoxicity is induced by paclitaxel chemotherapy in gastric cancer. Moreover, cardiovascular impairment is considered a main adverse effect of paclitaxel chemotherapy. Furthermore, polyphenolic compounds combined with anticancer drugs can improve therapeutic efficacy and decrease the systemic toxicity of chemotherapeutic agents.

This study evaluated the effect of consuming polyphenolic compounds on the cardiotoxicity induced by paclitaxel chemotherapy in gastric cancer.

Materials and Methods: We detected the critical hub genes network through artificial intelligence. Moreover, the signaling pathways and important biological mechanisms were identified based on the bioinformatic analysis. Furthermore, the vital biomarkers and hub genes involved in cardiotoxicity were detected. The chemoinformatic analysis revealed new compounds in Polyphenolic Bioactive Compounds (PBCs). In the experimental phases, mice were distributed into four groups (n=24), including Normal mice, mice treated with N-methyl-N-nitrosourea (MNU) (244 ppm, 18 weeks, GC group), GC mice received Paclitaxel (10 mg/kg, 7-day, GC+chemo group), GC mice received Paclitaxel and polyphenolic bioactive compounds (Apigenin (60 mg/kg/mice), Kaempferol (200 mg/kg/mice dissolved in 5% DMSO), Naringin (1250 mg/kg/mice), Gallic acid (200 mg/kg/mice) by gavage, 7-day, GC+PBCs group). The expression level of the hub genes was measured via qPCR Real-Time and ELISA methods.

Results: We anticipated a crucial hub gene related to the cardiotoxicity in GC mice that received Paclitaxel. Results designated that the myosin heavy chain b (b-MHC), Vascular Endothelial Growth Factor A (VEGF-A), sarcoplasmic reticulum Ca²⁺ ATPase (SERCA2), HMOX1 (heme oxygenase 1), and Atrial Natriuretic Factor (ANF) improved in GC+PBCs group compared with the other groups. Our data indicated that the expression level of genes related to the cardiotoxicity regulated in the GC mice received Paclitaxel and polyphenolic bioactive compounds. In addition, the troponin-c and natriuretic peptides (ANP) concentration ameliorated in the GC mice received Paclitaxel and polyphenolic bioactive compounds.

Conclusion: We found that consuming polyphenolic bioactive compounds improved the cardiotoxicity markers. Moreover, hub genes are recognized as druggable proteins for drug design and discovery approaches.

Keywords: Drug Design; Cardiotoxicity; Polyphenolic Bioactive Compounds, Hub Genes.



6th International TPCF Preclinical Imaging Symposium



MRI Contrast Agents: Advancements in Breast Cancer Imaging and Early Diagnosis

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Abstract

Background: The worldwide mortality of breast cancer emphasizes the significance of early diagnosis and treatment. Imaging detection is one of the tools utilized for screening, diagnosis, and treatment efficacy. In this study, we aimed to develop a novel tumor-targeting contrast agent for Magnetic Resonance Imaging (MRI) that enhances tumor visibility, thereby enabling more accurate identification and reducing general toxicity. To progress the tumor-targeting delivery of MRI contrast agents, we utilized a breast cancer-targeting peptide (referred to as VGB3) to prepare a peptide-functionalized based Gd-DTPA. The development of chemistry modification procedures has enabled the design and improvement of different peptide-based imaging agents with upgraded metabolic stability, favourable pharmacokinetics, improved binding affinity and selectivity, superior imaging ability as well and biosafety.

The primary objective of this study was to identify, describe, and evaluate the application of peptide-based MRI contrast agents in breast cancer imaging and early diagnosis.

Materials and Methods: The peptide was synthesized and Gd-DTPA was loaded onto the peptide. commercial Gd-DTPA, which served as the control, was purchased. Peptide-Gd-DTPA could recognize both Vascular Endothelial Development Factor Receptor (VEGFR)-1 and -2 within endothelial and 4T1 tumor cells (VEGFRS is overexpressed in breast cancer). Cytotoxicity and binding assay were performed. phantoms were prepared and imaged to measure 1/T1. For in vivo imaging, animals were injected with a dose (0.1 mg/kg) of peptide-Gd-DTPA and commercial Gd-DTPA with a Gd equivalent dose. T1 weighted were acquired, and Contrast to Noise Ratio (CNR) was measured.

Results: Peptide-Gd-DTPA showed no critical cytotoxicity to 4T1 mammary carcinoma cells (breast cancer cell line) and normal cells under the experimental conditions used. Compared with the commercial contrast agent (Gd-DTPA), peptide-Gd-DTPA showed higher T1 relaxation rates and superior tumor-targeting ability. peptide-Gd-DTPA displayed a greater accumulation in breast cancer cells than commercial contrast agent (Gd-DTPA), and an obvious increase in signal intensity was observed with peptide-Gd-DTPA compared with commercial contrast agent (Gd-DTPA).

Conclusion: The results illustrated that Peptide-Gd-DTPA specifically binds to 4T1 cancer cells with VEGFRS, which provides a novel MRI contrast agent with high specificity for breast cancer diagnosis, making it an exceptionally promising candidate for magnetic resonance imaging contrast improvement.

Keywords: Magnetic Resonance Imaging Contrast Agent; Peptide; Breast Cancer; Vascular Endothelial Development Factor Receptor.

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Evaluation of Proton Beam Dose Distribution in Breast Tissue Based on GATE Simulation Code

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Abstract

Background: The advantage of hadron therapy compared to radiation (photon) therapy is the lower integral dose for healthy tissues. The main reason for the increased interest in proton therapy is the physical characteristics of the dose-depth curve with a Bragg peak at a well-defined depth in the tissue.

In radiation therapy, treatment planning requires accurate assessment of the absorbed dose distribution in the target organs and tissues. GATE is an open source application based on the GEANT4 toolkit, which is potentially useful for a wide range of simulations, including dosimetry-related simulations. Since the simulation before the treatment plays a very important role in the quality of the treatment, in this research, the proton beam dose distribution in the breast phantom has been evaluated using the GATE simulation code.

Materials and Methods: In this research, vGATE.8.2 Monte Carlo code is used. The geometry used in the simulations is a multi-layered breast phantom with dimensions of 120×120×64mm, including a skin layer with a thickness of 2mm, a fat layer with a thickness of 5mm and a layer of breast tissue with a thickness of 57mm. The proton source is considered as a pencil beam (the output of a pencil scanning system) with a spot size of 3 mm and a divergence of 3 mrad. The emittance of the beam, which represents the area occupied by the particle in the phase space to check the quality of the used beam, is equal to 20 mm*mrad. The axis of the landing beam is considered in the Z direction. The physical list used is QGSP-BIC-EMY. Dose Actor was used to estimate the dose deposited in the phantom. The voxel size was set at 0.01cm in the beam direction. GATE simulations were performed with a total number of initial particles of 106. Statistical uncertainty of less than 1% was obtained.

Results: According to the thickness of the phantom, energy levels of 10-100 MeV were selected. By examining the dose-depth curves separately for single energy proton beams, at the beginning, with increasing depth, the dose increases slowly, but at the end of the range, the dose increase continues more sharply. As the particle's energy decreases, its movement speed becomes slower and its average energy decrease per unit length of the path increases. When the velocity of the particle approaches zero at the end of its range, the average energy loss is maximum. By comparing the Bragg curves with each other, it can be concluded that with the increase of energy from 10 MeV to 100 MeV, the width of the diagram and also the FWHM increase. As the energy of the proton beam increases, the peak of the Bragg curve is seen at a greater depth.

Conclusion: Therefore, proton beams can be used to destroy deep tumors so that the healthy tissue and organs at risk suffer less damage. In general, proton therapy is a useful treatment for growing organs in children and sensitive organs, but we should not ignore the effects of secondary particles that result from the collision of protons with materials.

Keywords: Proton Therapy; GATE Code; Bragg Peak; Dose Distribution.



A Framework for Tracking Human Pluripotent Stem Cells Transitions Using Time-Lapse Videos and Deep Learning

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Abstract

Background: Human pluripotent stem cells (hPSCs) offer a variety of clinical options in regenerative medicine and cell therapy. Considering complex relations of different factors associated with clonality, pluripotency, and differentiation pathways, current methods for hPSCs colony formation are inefficient and costly for large-scale clinical use of hPSCs. These challenges suggest the need for robust studies to comprehend existing data to develop more efficient and cheaper methods. The recent advances in the field of artificial intelligence and computer vision enable us to take a deeper look into cell behavior in vitro and to develop machine learning models for cell fate and transition which can shape the future of stem cell research and applications.

The present study identifies, tracks, and quantifies hPSCs transitions and movements in response to regenerative niche factors to deliver novel insights needed for filling the interpretation gaps, learning the relationships between different conditions, and making full use of the data we generate for future investigations.

Materials and Methods: We obtained time-lapse videos of hPSCs cultures recorded in the Stem Cell Biology Research Center, Shahid Sadoughi University of Medical Sciences. To analyze the recorded videos, we used a four-step deep learning-based: pre-training, annotation, fine-tuning and tracking. In the pre-training step, time-laps videos were converted to frames and uploaded on Robbofellow website, 40 images were manually annotated and used for pretraining a YOLO v8 model. The model learned to detect the bounding boxes of the cells in each frame. In the second step, the pre-trained model was used as an assistant to speed up the annotation process of half of the dataset. The model suggested the bounding boxes and we corrected them if needed. In the third step, we fine-tuned the pre-trained model on the annotated dataset from its last checkpoint. This improved the accuracy of the model. In the last step, we applied the fine-tuned model to the rest of the videos and tracked the cells over time. This allowed us to study the key properties of hPSCs such as correlated random walks, colony formation, and cell-cell distance.

Results: We developed a deep learning-based framework consisting of an annotation assistant and a final model for identifying and tracking hPSCs in culture, Which Iteratively results in improved tracking performance.

Conclusion: The framework developed in this study provides a novel approach for studying hPSCs behavior in vitro, applicable for future research in the field of stem cell and developing optimized colony formation methods suitable for large-scale clinical use of hPSCs.

Keywords: Mathematical Modelling; Human Pluripotent Stem Cells; Deep Learning, Tissue Regeneration; Cell Fate.



Advances in MRI Image Quality Enhancement Using Generative Adversarial Networks: A Literature Review

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Abstract

Background: Generative Adversarial Networks (GANs) represent a more recent advancement in the realm of deep learning, credited to the ingenuity of Ian Goodfellow and his collaborators. Gans constitute a class of deep learning models with the primary objective of generating novel images. The fundamental concept behind GANs involves a two-part adversarial framework: a generator and a discriminator. The generator aims to produce images that are indistinguishable from real ones, while the discriminator endeavors to differentiate between genuine and generated images. This adversarial interplay fosters a dynamic learning process where the generator continuously improves its ability to create convincing imagery.

The objective of this review article is to explore the applications of GAN models in enhancing the quality of Magnetic Resonance Imaging (MRI) images. By delving into the evolution and diverse applications of GAN.

Materials and Methods: This review investigates the diverse applications of GAN models in the enhancement of MNRI images. To achieve this, we employed a comprehensive literature search across relevant databases, including pubmed, and google scholar. Our search strategy involved querying for research articles, reviews, and relevant studies published up to the cutoff date of this review. The collected literature was then analyzed to identify key trends, methodologies, and outcomes pertaining to the utilization of GANs for MRI image quality improvement.

Results: In this comprehensive review, we have identified several remarkable applications of GANs in the field of MRI image enhancement. The key findings and insights from the reviewed literature are enhancing texture and resolution, novel network architecture (EAGAN), addressing noise, MRI augmentation and segmentation Multi Modal GAN(MM-GAN), multi-modal MRI image synthesis (GRMM-GAN), edge-enhanced Compressed Sensing MRI (CSMRI) reconstruction Edge-enhanced Dual Discriminator GAN (EDDGAN) these findings collectively highlight the immense potential of GANs in advancing the field of MRI image enhancement.

Conclusion: These findings collectively underscore the versatility and potential impact of GAN models in the field of MRI image enhancement. It is evident that GANs have become indispensable tools, offering novel solutions to address challenges in MRI data acquisition, reconstruction, and post-processing. The following section discusses the implications of these findings and the future directions in this burgeoning field.

Keywords: Generative Adversarial Networks; Magnetic Resonance Imaging; Image Enhancement; Generative Adversarial Networks.



6th International TPCF Preclinical Imaging Symposium



A Regional Effective Dose, Risk of Exposure-induced Death, and Annual Per Capita Dose in Diagnostic Radiology Procedures

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Abstract

Background: Ionizing radiation exposure doses during radiological procedures may increase the patient dose; therefore, dose assessment is an important subject. The current study aimed to estimate the Effective Dose (ED), Risk of Exposure-induced Death (REID), as well as Annual Per Capita Dose (APCD) in routine radiography procedures in Yazd province (Iran).

Materials and Methods: The data related to the exposure parameters and Entrance Surface Air Kerma (ESAK) of 9 public high-patient-load radiography centers (11 radiology devices) were collected from 783 patients. Five routine planar radiological examinations were included: lumbar spine, pelvis, abdomen, chest, and skull. The ED and REID values for each device and examination were obtained using a Personal Computer-based Monte Carlo (PCXMC, v. 2.0) software. The APCD was estimated by dividing the Annual Collective Effective Dose (ACED) to the Yazd population.

Results: The estimated mean ESAK values ranged from 0.26 ± 0.11 mGy (chest examination) to 8.45 ± 5.3 mGy (lumbar examination). The lumbar spine examination had the highest ED value (1.02 ± 0.75 mSv). The highest REID value for abdominal, chest, lumbar, pelvic, and skull examinations is associated with stomach (6.58 ± 7.72), lung (2.36 ± 2.79), stomach (7.03 ± 6.11), colon (3.31 ± 5.49), and other cancers (0.58 ± 0.56). The ACED value due to the radiology examinations was obtained at 45.782 man-Sv.

Conclusion: Our results demonstrated that the dose variations among the patients were remarkably high. Choosing appropriate imaging parameters, reducing the frequency of unnecessary radiology examinations, and performing quality control procedures of radiology machines could reduce the patients' doses.

Keywords: Radiography; Entrance Surface Air Kerma; Effective Dose; Cancer Mortality; Annual Per Capita Dose.



An Analysis of the Rate and Reasons of Rejected Radiographs in Emergency and Non-Emergency Radiology Departments in Yasuj, Iran

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Abstract

Background: Utilizing imaging to improve physicians' diagnostic accuracy is one of the primary priorities of radiology departments. When the image is of poor quality, it is likely to be rejected, and its repetition will expose patient and staff to unnecessary ionizing radiation. Given the significant nature of this issue, the aim of the current study was to evaluate the rate and reasons of radiograph rejections in emergency (public practice) and non-emergency (private practice) radiology departments of Yasuj, Iran.

Materials and Methods: This cross-sectional study was carried out over a 14-day period in Yasuj, Iran, in the accident and emergency (round-the-clock) and non-emergency (day) medical imaging departments. In terms of quality, a total of 7006 images were classified in the following three grades; A (Good), B (Fair) and C (rejected). The grade C radiographs were categorized into 9 classes according to the reasons of rejection.

Results: During this study, 7006 radiographs were examined, of which 6458 (92.2%) were categorized as grade A. Additionally, 401 radiographs (5.7%) were categorized as grade B, and 147 radiographs (2.1%) were considered to be grade C, which means that they were rejected. Out of the rejected radiographs, 69 (1.9%) were from emergency departments, while 78 (2.3%) were from non-emergency radiology departments. The most common reasons for the rejection of radiographs were the patient's incorrect positioning in 45 cases (30.6%) and the patient's motion in 43 cases (29.3%).

Conclusion: In comparison to previous research, the current study's percentage of rejected images was deemed acceptable at 2.1%. Radiologists are advised to frequently assess the reason and rate for rejecting radiographs to enhance the effectiveness of their radiology unit.

Keywords: Image Rejection; Computed Radiography; Digital Radiography; Quality Assurance; Image Quality, Image Reject Analysis.



6th International TPCF Preclinical Imaging Symposium



Radio Protective Effect of Black Mulberry Extract on Radiation-Induced Damage in Bone Marrow Cells and Liver in the Rat

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Abstract

Background: Ionizing radiation by producing free radicals induces tissue oxidative stress and has clastogenic and cytotoxic effects.

The radioprotective effect of Black Mulberry Extract (BME) has been investigated on liver tissue and bone marrow cells in the rat.

Materials and Methods: 200 mg/kg BME injected intraperitoneally to the forty-eight male wistar rats three days before and three days after 3 Gy and 6 Gy gamma irradiation, The frequency of Micronucleated Polychromatic Erythrocytes (MnPCEs), Micronucleated Normochromatic Erythrocyte (MnNCEs) and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte +normochromatic erythrocyte) were calculated. In addition, the level of malondialdehyde (MDA) and Superoxide Dismutase (SOD), total thiol content and catalase activity was determined in rat's liver.

Results: BME significantly reduced the frequencies of MnPCEs and MnNCEs and increased PCE/PCE + NCE ratio in rat bone marrow compared to the non-treated irradiated groups. Moreover, this concentration of BME extract decreased the level of MDA and SOD, as well as enhanced the total thiol content and catalase activity in rat's liver compared to the non-treated irradiated groups.

Conclusion: It seems that BME extract with antioxidant activity reduced the genotoxicity and cytotoxicity induced by gamma irradiation in bone marrow cells and liver in the rat.

Keywords: Black Mulberry; Ionizing Radiation; Micronucleus; Bone Marrow cells; Liver Parameters.



Origanum Vulgare Leaf Extract Protects Mice Bone Marrow Cells Against Ionizing Radiation

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Abstract

Background: Ionizing radiation produces free radicals which induce DNA damage and cell death. Origanum Vulgare Leaf Extract (OVLE) is a natural compound and its capability of scavenging free radicals and its antioxidant activity have been demonstrated by many researchers. In this study, using micronucleus assay, radioprotective effect of OVLE against clastogenic and cytotoxic effect of gamma irradiation has been investigated in mice bone marrow cells.

OVLE was injected intraperitoneally to the BALB/c mice 1hr prior to gamma irradiation (3Gy) at the doses of 100 and 200 mg/kg. Twenty four hours after irradiation or treatment, animals were killed and smears were prepared from the bone marrow cells. The slides were stained with May Grunwald–Giemsa method and analyzed microscopically. The frequency of Micronucleated Polychromatic Erythrocytes (MnPCEs), Micronucleated Normochromatic Erythrocyte (MnNCEs) and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte + normochromatic erythrocyte) were calculated.

Materials and Methods: 200 mg/kg BME injected intraperitoneally to the forty-eight male wistar rats three days before and three days after 3 Gy and 6 Gy gamma irradiation, The frequency of, MnNCEs and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte +normochromatic erythrocyte) were calculated. In addition, the level of malondialdehyde (MDA) and Superoxide Dismutase (SOD), total thiol content and catalase activity was determined in rat's liver.

Results: The results showed that gamma irradiation (3Gy) increased the frequency of MnPCEs, MnNCEs and reduced the PCE/PCE+NCE ratio in mice bone marrow compared to the non-irradiated control group ($p < 0.0001$). Injection of OVLE significantly reduced the frequency of MnPCEs ($p < 0.0001$) and MnNCEs ($p < 0.05$) and increased the PCE/PCE+NCE ratio as compared to the irradiated control group ($p < 0.05$).

Conclusion: It seems that OVLE with its antioxidant properties and its capability of scavenging free radicals and reactive oxygen species can reduce the cytotoxic effects of gamma irradiation in mice bone marrow cells.

Keywords: Radioprotective Agents; Micronucleus; Bone Marrow Cells; Whole-body Irradiation; Origanum Vulgare.



6th International TPCF Preclinical Imaging Symposium



Radiomics in Medical Imaging: A Digital Biopsy

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Abstract

Background: In recent years, radiomics has gained significant popularity in clinical research. This quantitative approach to medical imaging leverages advanced mathematical analyses to convert images into data, with the goal of offering medical professionals more precise and efficient information. Through the extraction and analysis of subtle image features from medical images to identify tissue and pathological changes, radiomics enables accurate disease diagnosis and continuous monitoring.

The term "Radiomics" denotes the process of extracting and analysing copious amounts of advanced quantitative imaging features from medical images obtained through Computed Tomography (CT), Positron Emission Tomography (PET), or Magnetic Resonance Imaging (MRI) techniques. It is critical to note that these data are meant to be extracted from standard-of-care images, thereby leading to a vast potential subject pool. Radiomic data can be mined effectively to construct both descriptive and predictive models that relate image features with phenotypes or gene-protein signatures. In medicine, various ways to generate big data exist, including the widely known fields of genomics, proteomics, or metabolomics. Similar to these "omics" clusters, imaging has been used increasingly to generate a dedicated omics cluster itself called "radiomics". Radiomics is a quantitative approach to medical imaging, which aims at enhancing the existing data available to clinicians by means of advanced, and sometimes nonintuitive mathematical analysis. In essence, the fundamental hypothesis of radiomics is that these models, which may incorporate biological or medical data, can provide valuable diagnostic, prognostic, or predictive information. The radiomics endeavour can be split into different processes, each with its unique challenges that require overcoming, including (i) image acquisition and reconstruction, (ii) image segmentation and rendering, (iii) feature extraction and qualification, (iv) databases and data sharing for eventual (v) ad hoc informatic analyses. Each of these processes presents particular challenges that must be addressed.

Materials and Methods: In this review article the keywords were Radiomics, Image features, Quantitative imaging biomarkers, Artificial intelligent and Machine learning based on PubMed, Scopus and Google scholar databases during the 2010- 2023s. Then, the information is collected by selecting featured articles.

Results: Several studies showed that radiomics is very promising. Radiomics are quantifiable features that are extracted from medical imaging data. These features are based on imaging features including pixel intensity, pixel arrangement, pixel color and texture. This method extracts quantitative data that are not detected by human eye. (In practice, visual analysis manages to extract only about 10% of the information contained in a digital medical image).

Conclusion: I came to the conclusion that despite all the challenges facing this field of science and its entry into the field of medical imaging, it can produce remarkable results. in the diagnosis and follow-up of various diseases, including cancer.

Keywords: Radiomics; Image Features; Quantitative Imaging Biomarkers; Artificial Intelligent.



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The Effects of Chronic Noise Exposure on Hippocampal Neurons in Wistar Rat

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Abstract

Background: Chronic noise exposure may lead to neural hippocampus apoptosis. Also stresses may result in dark neurons.

The aim of this study was to determine effects of chronic noise on the hippocampus neurons of exposed rats.

Materials and Methods: In this study 16 male Wistar rats were divided randomly into 2 groups, including exposure (N) and control (C) groups. 30 days after onset of examination, skulls of rats were opened to remove their brains. TUNEL and Toluidine blue techniques were used for examination of samples. The number of TUNEL positive and dark neurons in the hippocampus of both groups was counted and were compared.

Results: In comparison with control group, in hippocampus of exposed rats neural apoptosis and dark neurons were increased considerably ($P < 0.05$).

Conclusion: Apoptosis and dark neuron in hippocampus of rats can be caused by exposure to chronic noise.

Keywords: Chronic Noise; Broad Band (White) Noise; Hippocampus; Apoptosis; Dark Neuron .



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Effectiveness of Contrast Agents and Molecular Indicators in Alzheimer's Diagnosis Through PET and SPECT Imaging on Animal Models

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Abstract

Background: The importance of cognitive decline has increased due to an aging population and changing lifestyles. Currently, an absolute diagnosis of Alzheimer's Disease (AD) can only be determined through postmortem histopathological examination, although in vivo imaging is making strides towards this diagnosis. Upon examining the postmortem brains of AD patients, the disease is associated with neuropathological features such as the accumulation of amyloid β ($A\beta$) plaques, also known as senile plaques, and neurofibrillary tangles (NFT) of highly phosphorylated tau in the brain. Early detection and diagnosis of Alzheimer's disease are crucial, but current research on the effectiveness of contrast agents and molecules is limited. To address this gap, we conducted a comprehensive study on Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) imaging to evaluate the role of these agents and indicators in diagnosing the disorder.

Investigating the effectiveness of contrast agents and effective molecular indicators in Alzheimer's diagnosis through PET and SPECT imaging on animal models.

Materials and Methods: A comprehensive search was conducted in PubMed, using the PRISMA guidelines, without any time or language restrictions. Three independent researchers reviewed the studies based on criteria, and relevant data from the included articles were extracted and analyzed.

Results: As a result of the initial search, 172 original articles were included in the study. Finally, data from 116 studies were extracted. 30 studies (35.3%) have been conducted in the last five years. 110 studies (94.8%) worked on Alzheimer's, and the others worked on neurological diseases, including dementia. On average, 23 animals were used in each study. 67 studies (57.8%) made use of [¹⁸F] fluorodeoxyglucose and its derivatives as the contrast agent; 18 studies (15.5%) used [¹¹C] acetate; 10 studies (8.6%) used chemicals based on iodine; and 20 (17.2%) used other contrast agents. At last, 109 studies (94%) reached an eligible outcome.

Conclusion: It's crucial to recognize some of the study's shortcomings. First off, since only animal models were used, there's a chance that the results won't apply equally well to people. The efficacy of these contrast agents and molecular markers in clinical settings requires more study. Future research should take into account the fact that the study did not evaluate the long-term consequences or safety of the contrast agents employed. In order to confirm these results in clinical settings and to evaluate the long-term impact and safety of the contrast chemicals utilized, more investigation is required. According to this research, PET and SPECT imaging might be useful diagnostic methods for Alzheimer's disease when used in conjunction with the right contrast agents and molecular markers. Overall, this research advances our knowledge of diagnosing Alzheimer's disease and sets the door for more development in this area.

Keywords: Alzheimer's Disease; Single Photon Emission Computed Tomography; Positron Emission Tomography.

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Curcumin Loading Potentiates the Neuroprotective Efficacy of Fe₃O₄ Magnetic Nanoparticles in Cerebellum Cells of Schizophrenic Rats

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Abstract

Background: The aim of this study was to investigate the neurotoxic effects of Fe₃O₄ magnetic- CurNPs on isolated schizophrenia mitochondria of rats as an in vivo model.

Materials and Methods: We designed CMN loaded superparamagnetic iron oxide nanoparticles (SPIONs) (Fe₃O₄ magnetic- CurNPs) to achieve an enhanced therapeutic effect. The physicochemical properties of magnetic- CurNPs were characterized using X-Ray Diffraction (XRD), and Dynamic Laser light Scattering (DLS) and zeta potential. Further, to prove Fe₃O₄ magnetic- CurNPs results in superior therapeutic effects, and also, the mitochondrial membrane potential collapse, mitochondrial complex II activity, reactive oxygen species generation, ATP level, cytochrome c release and histopathology of cerebellums were determined in brains of schizophrenic rats.

Results: We showed that effective treatment with CMN reduced or prevented Fe₃O₄ magnetic-induced oxidative stress and mitochondrial dysfunction in the rat brain probably, as well as mitochondrial complex II activity, MMP, and ATP level were remarkably reduced in the cerebellum mitochondria of treated group toward control ($p < 0.05$). Therewith, ROS generation, and cytochrome c release were notably ($p < 0.05$) increased in the cerebellum mitochondria of treated group compared with control group. Taken together, Fe₃O₄ magnetic- CurNPs exhibits potent antineurotoxicity activity in cerebellums of schizophrenic rats. This approach can be extended to preclinical and clinical use and may have importance in schizophrenia treatment in the future.

Conclusion: To our knowledge this is the first report that provides the Fe₃O₄ magnetic- CurNPs could enhance the neuroprotective effects of CMN in the Schizophrenia.

Keywords: Schizophrenia; Curcumin; Mitochondrial; Iron Oxide Nanoparticles; Oxidative Stress.



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Selective Cytotoxicity Mechanisms and Biodistribution of Diamond Nanoparticles on the Skin Cancer in C57 Mouse

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Abstract

Background: The cytotoxicity of Diamond Nanoparticles (DNs) to various cell lines has been on focus by numerous scientists. The cellular toxicity system of DNPs has not been fully understood or explained in skin cancer, at this point.

Materials and Methods: This research was carried out to discover and reveal the potential impacts of DNPs on the secluded brain, heart, liver, kidney, and skin in addition to evaluation of their cytotoxicity mechanism under test conditions. Their biological activities, for example cell viability, the level of Reactive Oxygen Species (ROS), lipid peroxidation, cytochrome c release and Apoptosis/Necrosis were evaluated. Additionally, the bio-distribution of these nanomaterials in tissues was examined in the C57 mouse.

Results: Relying on the findings of the investigation, DNPs were found to increase the ROS level, Malondialdehyde (MDA) content, release of cytochrome c, and cell death in skin significantly compared to other groups. In the C57 mouse, DNPs were observed to have accumulated in skin tissue more intensively than they did in other organs.

Conclusion: The present study presents for the proof that DNPs can completely induce cell death signaling in skin cancer without bringing about a high cytotoxicity in other tissues. Results suggest that DNPs can be valuable in recognition of skin cancer.

Keywords: Cytotoxicity; Reactive Oxygen Species; Cytochrome C Release.



6th International TPCF Preclinical Imaging Symposium



Small Magnets, Big Future: Low-Field MRI Technology and Clinical Utility

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Abstract

Background: Magnetic Resonance Imaging (MRI) is an indispensable medical imaging modality that has revolutionized the non-invasive assessment of soft tissue morphology and anatomy. Conventionally, clinical MRI scanners operate at high static magnetic field strengths of 1.5 Tesla (T) or above. Conversely, lower-field open MRI systems using between 0.2-0.5T have also been developed to address specific needs in the Medical Imaging Field. Low-field MRI (LF-MRI) has several advantages over high-field units. Mainly, it enables the scanning of claustrophobic or anxious patients especially small children who cannot tolerate standard high-field enclosed scanners due to feelings of discomfort. The open bore configuration of LF-MRI alleviates such issues by providing a more spacious examination environment. Additionally, the lower static magnetic field and reduced radiofrequency power deposition permit metallic and electronic medical devices to be safely imaged, expanding clinical applications. While image quality tends to be degraded relative to high-field MRI due to a lower signal-to-noise ratio, technological advances have helped offset this limitation for better outcomes in the near future. This review aims to provide a comprehensive outline of the current applications, technical aspects, and evidence supporting the diagnostic accuracy of Low-Field MRI.

Materials and Methods: A systematic search of the literature was conducted using Google Scholar and PubMed databases to identify relevant studies published on low-field MRI since 2021. The search strategy involved entering the key term "low field MRI" in the title field and limiting results to articles published from 2021 to the present. This initial search yielded 156 articles from Google Scholar and 63 articles from PubMed. After removing duplicate articles found in both databases, the total number of unique articles was 178. The titles and abstracts of these 178 articles were screened for relevance to the topic of low-field MRI technological advances, techniques, clinical applications, and comparisons to high-field strength MRI. Studies were excluded if they focused solely on high-field MRI without discussion of low-field systems, were not published in English, or were conference abstracts or proceedings without full text available. The application of these exclusion criteria left a total of 51 relevant original research and review articles to be included in the analysis.

Results: The Results showed that the portable structure expands the availability of MRI beyond fixed facilities. One study indicated that Low-field MRI at 0.55 T may have similar accuracy as 1.5 T scanners for the detection of micro bleeds and thus has great potential as a resource-efficient alternative in stroke diagnosis. One study on the prostate suggested that low-field MRI offers a cost-efficient alternative to the high-field MRI for prostate cancer diagnosis. A study suggested that both low-field and high-field MRI can identify the meningeal involvement in SRMA and inflammation of surrounding tissues with good diagnostic capability. The literature dictated the utility of low-field MRI in many applications such as: musculoskeletal, breast, and abdominal imaging.

Conclusion: In conclusion, these studies demonstrate the potential of low-field MRI as a cost-efficient alternative to high-field MRI for several clinical applications. The reduced costs and accessibility afforded by low-field designs, positions this technology to increase diagnostic MRI access globally. However, further validation of diagnostic performance and cost-utility analyses accounting for accuracy are still needed.

Keywords: Portable Magnetic Resonance Imaging; Low Field Magnetic Resonance Imaging; Ultra Low Field Magnetic Resonance Imaging; Artificial Intelligence in Low Field Magnetic Resonance Imaging.



6th International TPCF Preclinical Imaging Symposium



Quantitative Online Imaging of Oxygen Concentration during Radiobiological Studies on Small Animals with Proton Beams Using a Slit-Slat Prompt Gamma Camera: A Monte Carlo Simulation Study

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Abstract

Background: Prompt gammas could be used for online non-invasive monitoring the early phase of tumor oxygenation during radiobiological studies using proton beam irradiation.

In this study, a slit-slat prompt gamma camera was optimized and evaluated for oxygenation imaging.

Materials and Methods: In this review article the keywords were Radiomics, Image features, Quantitative imaging biomarkers, Artificial intelligent and Machine learning based on PubMed, Scopus and Google scholar databases during the 2010- 2023s. Then, the information is collected by selecting featured articles.

Results: It was found that there is a good correlation between oxygen concentration and the detected PGs using the slit-slat camera (Pearson's $r = 0.9997$). Using the derived formula, the amount of oxygen mass in the test sample was estimated as 276.0 ± 73.0 mg (26% relative error) for a real oxygen concentration of 280.0 mg.

Conclusion: It was demonstrated that the suggested imaging system could provide an image of the oxygen concentration in the sample. As a result, a slit-slat camera might be used to measure and monitor variations in oxygen levels in irradiated tumors during proton treatment.

Keywords: Oxygenation Imaging; Radiobiology; Gamma Camera; Monte Carlo; Small Animal Imaging; Proton Beam.



Radioprotective Effect of Amifostine in Head and Neck Radiotherapy Against Osteoradionecrosis of the Mandible

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Abstract

Background: Head and Neck Cancer (HNC) ranks as the seventh most prevalent form of cancer globally. The standard treatment modalities for cancer patients often encompass surgical resection of the tumor, administration of chemotherapy agents, and utilization of radiation. Radiotherapy is widely utilized as a primary treatment modality for HNC. While radiation has been shown to enhance disease management and extend overall life rates, it is important to note that treatment may also result in detrimental effects on neighboring healthy tissue, such as bone loss. Osteoradionecrosis (ORN) of the mandible is a frequently seen form of bone radiation injury. Amifostine (AMF) is a prodrug that protects normal tissues from radiation damage while maintaining radiotherapy's effectiveness. It forms an active thiol compound through dephosphorylation in endothelial cells. Research on animals shows that administration AMF before radiotherapy can maintain mandible bone biomechanical characteristics and reduce the risk of ORN development.

The objective of this study was to examine the effectiveness of AMF in the context of HNC irradiation for the treatment of ORN of the mandible in animal specimens.

Materials and Methods: This review article evaluates the effectiveness of AMF in treating HNC radiation using a comprehensive review of scholarly material from pubmed and google scholar databases. The study aimed to identify patterns, approaches, and results in the use of AMF in addressing bone-related issues, based on research papers, reviews, and published studies. The evaluation aims to provide a comprehensive understanding of the potential benefits of AMF in treating bone-related conditions.

Results: This study aimed to comprehensively examine the efficacy of AMF administered prior to radiation. The literature research revealed significant data indicating that the administration of subcutaneous injections of AMF to rats before to each radiotherapy session can effectively mitigate radiation-induced damage in the skeletal system. Various methodologies have been employed in diverse investigations to assess the efficacy of AMF against ORN. These methodologies encompass histological analysis, biomechanical testing, evaluation of bone mineral density distribution, micro-computed tomography scan and spectroscopic techniques. The experimental findings indicate a decrease in the ORN in the mandible of rats treated with AMF injections. While AMF does possess radioprotective properties, its administration in humans is limited due to the presence of adverse effects such as nausea, vomiting, and hypotension.

Conclusion: Radiation-induced bone diseases give rise to substantial problems. At now, there exists a lack of efficacious preventative measures. The aforementioned data underscore the efficacy of AMF in mitigating the ORN. By extrapolating these results to human subjects, it is possible to partially mitigate the adverse consequences associated with radiation treatment. The utilization of radioprotectors, such as AMF, has been shown to effectively mitigate the adverse effects of radiation on healthy tissues in close proximity to tumor tissues.

Keywords: Radioprotector; Amifostine; Head and Neck Cancer.



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Recent Advances in Medical Imaging and Deep Learning with Transformer for Breast Cancer Diagnosis: MRI, CT, and PET Scans

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Abstract

Background: Breast cancer is a multifaceted disease that ranks as the second leading cause of cancer-related mortality in women. The early-stage diagnosis of breast cancer patients is a crucial component of breast cancer treatment. Among the different diagnostic platforms available, imaging techniques are considered the primary diagnostic tools that can yield significant data for individuals diagnosed with breast cancer. Multiple imaging modalities, including Positron Emission Tomography (PET), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), have demonstrated their potential utility in the diagnosis and monitoring of patients at different stages of breast cancer. Deep learning algorithms exhibit considerable potential in the field of breast cancer imaging, namely in the areas of tumor detection, segmentation, and outcome prediction through the utilization of MRI, CT, and PET images. The utilization of advanced deep learning techniques, such as transformer models, has significantly augmented the capabilities of image processing. A comparative analysis between deep learning and classical methodologies, together with an examination of their respective advantages and limitations, elucidates their complementary functions within the realm of cancer care.

The purpose of this study is to provide researchers and clinicians with an overview of the advancements, possibilities, and challenges associated with the utilization of deep learning techniques using transformer models in the field of breast cancer imaging. The ultimate objective is to offer guidance for future research endeavors that might enhance patient outcomes and facilitate the development of individualized treatment approaches.

Materials and Methods: This paper examines the utilization of imaging modalities in the detection of breast cancer, specifically in conjunction with deep learning models using transformers. The study conducted a comprehensive literature review using databases like PUBMED and Google Scholar, using queries to retrieve research papers, reviews, and studies up to the specified cut-off date. The gathered material was then analyzed to identify significant patterns, approaches, and results related to the use of transformers in specific imaging modalities.

Results: Transformer models are used to analyze breast cancer images in this study. We found two key components in our investigation. First, advanced medical imaging tools like MRI, CT, and PET scans help detect and monitor breast cancer. These methods improve diagnosis accuracy and offer individualized therapy options. Deep learning transformer models may improve tumor identification, segmentation, and prediction based on these images. These novel methods can improve patient outcomes and enable tailored breast cancer treatment. Combining advanced imaging technologies with deep learning algorithms may improve breast cancer diagnosis and treatment.

Conclusion: Advancements in medical imaging and deep learning transformer models have shown promising potential for improving breast cancer outcomes. Advanced imaging technologies like MRI, CT, and PET scans enable more precise and comprehensive detection of breast cancer, enabling early diagnosis and better treatment options. Deep learning transformer models can predict patient prognosis and aid healthcare professionals in determining optimal treatment strategies. The integration of these techniques with deep learning algorithms could significantly improve breast cancer patient outcomes and lead to the development of more effective therapies in the future.

Keywords: Breast Cancer; Deep Learning; Transformer.



Assessing the Value of FDG-PET in Cancer Diagnosis and Staging: A Narrative Review

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Abstract

Background: Cancer remains a major global health burden, representing a heterogeneous group of diseases characterized by uncontrolled cell growth. Effective diagnosis and assessment of cancer extent are crucial for determining appropriate treatment and monitoring outcomes. Conventional imaging modalities have limitations in detecting small tumors, differentiating malignant from benign lesions. Positron Emission Tomography (PET) has emerged as a powerful functional imaging modality to address some of these diagnostic challenges faced in oncology. 2-deoxy-2-[¹⁸F] fluoro-D-glucose (¹⁸F-FDG) is a glucose analog that is actively transported into cells and phosphorylated, malignant tumors tend to demonstrate elevated glucose metabolism and increased FDG uptake compared to normal tissue. As malignant tumors often exhibit increased expression of glucose transporters and increased glycolytic rates, they appear as focal areas of increased FDG accumulation on PET scans. This facilitates detecting primary tumors as well as metastatic diseases that may be occult on anatomical imaging alone.

This review aims to summarize the current evidence base regarding the applications of FDG-PET in the diagnosis and management of cancer patients.

Materials and Methods: A search of the literature was conducted to identify relevant studies on this topic. The scientific databases Google Scholar and Science Direct were searched using the following search strategy: “Fluorodeoxyglucose-Positron emission tomography” or “FDG-PET” in the title field of the article and “diagnosis” or “detection” and “cancer” in all text fields. This search strategy was aimed at capturing studies assessing diagnostic applications of FDG-PET or FDG-PET/CT for cancer. Limits were placed to retrieve articles published from 2022 to the present to ensure that recently published literature was reviewed. Records were excluded if they were: reviews/editorials/case reports, letters/abstracts only, non-English language, or involved non-human subjects. Two independent reviewers screened all retrieved titles and abstracts to identify relevant papers for full-text review.

Results: The initial search resulted in 17,600 records. The search and screening process identified 21 primary studies deemed eligible for inclusion in the narrative review. One study examining the ability of FDG-PET to detect recurrent or residual lung cancer found a sensitivity of 100% (26/26) and specificity of 61.5% (8/13), indicating FDG-PET is highly sensitive but has moderate specificity for detecting lung cancer recurrence or residuals. FDG-PET can help precisely stage pediatric soft-tissue sarcoma patients, particularly for detecting lymph node metastases, and may be considered in their initial workup. FDG-PET/CT plays an important role in identifying the gross tumor volume for radiotherapy planning of anal and rectal cancers. Several meta-analyses and reviews concluded that FDG-PET is clinically useful for detecting cancers, differentiating malignant and benign lesions (over 90%), cancer staging, assessing cancer therapy response, and detecting recurrence for many cancer types, including lung, gastrointestinal, breast cancers, and lymphomas.

Conclusion: The studies presented provide strong evidence that FDG-PET is a highly sensitive imaging modality for detecting a variety of cancers across multiple anatomical sites. FDG-PET is clinically useful for detecting cancers, cancer staging, assessing cancer therapy response, and detecting recurrence for many cancer types.

Keywords: Cancer; Fluorodeoxyglucose-Positron Emission Tomography; Diagnosis.



6th International TPCF Preclinical Imaging Symposium



Melatonin-induced Alterations in Bax Gene Expression in Non-obstructive Azoospermic Mice

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Abstract

Background: Non-Obstructive Azoospermia (NOA) represents a formidable challenge in addressing male infertility, characterized by its limited treatment prospects. This research explores the potential impact of melatonin administration on the expression levels of critical genes such as DAZL, Stra8, Sycp3, Bax, and VASA.

Exploring the therapeutic efficacy of melatonin in non-obstructive azoospermia balb/c mice following busulfan treatment.

Materials and Methods: Eighteen adult mice were allocated into three distinct experimental cohorts: (1) Sham group, (2) Busulfan receiving group (NOA model), and (3) NOA+ Melatonin treatment group. Melatonin was administered intraperitoneally (IP) at a dosage of 8 mg/kg per week, commencing after the confirmation of azoospermia induction and continuing for eight weeks. Subsequently, the animals were euthanized, and testicular samples were collected for subsequent analysis.

Results: The results indicated a significant reduction in the expression of Bax compared to the untreated group. Additionally, the expression levels of DAZL, Vasa, and Stra8 genes exhibited an upward trend compared to the azoospermic group, although statistical significance was not reached. Notably, the expression of the Sycp3 gene remained unaltered relative to the untreated group. These observed distinctions were further validated through quantitative real-time polymerase chain reaction (qRT-PCR) analysis.

Conclusion: Our study underscores melatonin therapy's substantial impact on diminishing the pro-apoptotic Bax gene expression in non-obstructive azoospermic mice. Additionally, melatonin can augment gene expression associated with spermatogenesis, meiosis, and germ-cell development. Nonetheless, it is essential to note that melatonin may not fully alleviate the state of azoospermia when administered alone.

Keywords: Male Infertility; Non-Obstructive Azoospermia; Melatonin; Spermatogenesis; Gene Expression.



Swine Teeth as a Radiodensity Model for Human Odontology: A Review Article

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Abstract

Background: Several animal teeth have been used in laboratory tests with the assumption that they exhibit similarities with human teeth. Although various studies have been carried out to compare animal to human teeth, no conclusive studies have yet warranted the use of animal teeth in laboratory tests. The primary criterion for the selection of teeth of different species is their structural and physicochemical properties. Swine teeth are also used as substitutes for human teeth in studies of adhesion and amelogenesis, because they are more similar to human teeth than the teeth of other mammals in relation to shape, size, morphology and period of development. In addition, some enamel proteins used for periodontal therapy are extracted from swine tooth germs because it is considered that composition of swine enamel is similar to human enamel. On the other hand, swine teeth are higher and more complex in shape than human teeth, having a greater number of cusps and irregularities. Studies showed that swine teeth are less resistant to fracture under compressive forces in comparison with human teeth, which is probably due to their thinner enamel.

The present work stands out because of its originality, since when doing a bibliographic search; we have found just a few references about pig species, where all the anatomical references, morphology, physiology, classification, descriptive elements and work model for teeth in pig are described in such a detailed way.

Materials and Methods: A detailed search has been done on Google scholar and PubMed for identification of research papers related to swine teeth and human odontology. The important research works found during the manual search were also gathered in this review. During search, some keywords such as “odontology” or “human” or “radiodensity” or “swine teeth” or “dentin and enamel” or “imaging” were used.

Results: The photoelectric effect is considered to be an example of the absorption phenomena. The Compton effect is an example of the scattering phenomena and approximately 62% of the photons undergo Compton interactions. Irrespective of the type of X-ray-to-matter interactions, it is always directly proportional to either the atomic number of the absorber or to its electric density. Thus, depending on the atomic composition of the matter, the radiodensity of a radiographic image will be differently influenced. At this point, literature is too contradictory. Some authors state that all mammalian teeth are essentially similar but the trace element concentration in the enamel of human and swine teeth are similar to each other. The form of the pulp cavity resembled the shape of the tooth as in human teeth.

Conclusion: Based on the findings of selected articles in this review, inconsistent data exist regarding that swine teeth can be considered appropriate substitute for human teeth, in the reviewed fields of dental research with many of the characteristics of the ideal animal in dental research, such as: similar growth rate, physiology and suitable size of teeth and mandible to allow dental operations and growth measurements.

Keywords: Swine; Teeth, Human; Radiodensity; Imaging, Odontology.



Comparison of Single and Two-Layer Tapered MicroPET Scanner with Default Cuboidal Scanners

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Abstract

Background: Animals play an important role in medical research, leading to the development of dedicated small animal PET scanners. These advancements highlight the demand for high-resolution systems capable of imaging the small structures and subtle lesions within small animals. Considering the very small size of organs in small animals, often in the submillimeter range, these systems are commonly referred to as microPETs. One strategy to enhance image quality in microPETs involves reducing the diameter of PET rings. Reducing the ring diameter of cuboidal microPETs introduces gaps that diminish system sensitivity. Consequently, tapered array detectors have emerged to address this challenge by filling these gaps. Moreover, the role of crystal materials and the configuration of detector layers have gained significant attention in optimizing scanner performance. In this study, we assess four systems: cuboidal and tapered array systems with single layers, and their phoswich counterparts. We evaluate parameters such as sensitivity, scatter fraction, Noise Equivalent Count Rate (NECR), and energy resolution.

Materials and Methods: Scanners with conventional cuboidal detectors consist of 16 detectors, each with dimension of $6.95 \times 12.05 \times 13 \text{ mm}^3$. Each detector contains a 14×14 crystal array with dimension of $0.45 \times 0.814 \times 13 \text{ mm}^3$. The tapered array detectors share the same front-face dimensions but differ on the rear face, with dimensions of $6.95 \times 16.05 \text{ mm}^2$ for detectors and $0.45 \times 1.1 \text{ mm}^2$ for crystals. Single-layer detectors use LSO crystal materials, while phoswich systems combine LSO crystals at the front and BGO crystals at the rear. Monte Carlo GATE simulation tools were employed. An energy window spanning 150-700 keV and a 20 nanosecond coincidence time window were set. A spherical source with a diameter of 0.5 mm and an activity of 400 kBq was simulated at the center of field of view.

Results: The sensitivity of single-layer cuboidal, single-layer tapered, phoswich cuboidal, and phoswich tapered detectors is 1.3%, 1.5%, 1.3%, and 1.6%, respectively. Single-layer and phoswich tapered detectors exhibit approximately 19% and 24% higher sensitivity than single-layer cuboidal detectors. Moreover, Phoswich tapered detectors exhibit 4% greater sensitivity than single-layer tapered ones. Scatter fraction is negligible in all scanners and is zero in the phoswich tapered detector. Regarding NECR, both single-layer tapered and phoswich tapered detectors outperform the cuboidal detector by 19% and 29%, respectively. The NECR of the phoswich tapered detector is 9% higher than that of the single-layer tapered detector. Energy resolution for single-layer scanners is 26.74%. Phoswich cuboidal and phoswich tapered scanners attain energy resolutions of 24.9% and 24.2%, indicating 7% and 9% improvements over single-layer systems, respectively.

Conclusion: In terms of sensitivity and NECR, no notable difference exists between single-layer and phoswich cuboidal detectors. In contrast, the tapered detectors outperform cuboidal ones in both sensitivity and NECR. Remarkably, even the phoswich tapered detector surpasses the single-layer tapered detector in these aspects. Enhanced energy resolution in phoswich systems may be attributed to the inclusion of BGO crystals. Furthermore, the larger BGO area on the back face of tapered arrays may contribute to the slightly improved energy resolution in phoswich tapered scanners in comparison to cuboidal scanners.

Keywords: Micro Positron Emission Tomography; Tapered Detectors; Phoswich.

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6th International TPCF Preclinical Imaging Symposium



Brain Function Analysis During Sleep Deprivation to Suggest fMRI Imaging Biomarkers Related to Insomnia

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Abstract

Background: A physician diagnoses insomnia using a clinical examination of the patient and an insomnia questionnaire. However these methods have problems such as being subjective and dependent on the therapist and the patient's mood.

This study aimed to examine the brain maps of young and older adults during sleep deprivation and propose fMRI imaging biomarkers to diagnose insomnia.

Materials and Methods: Forty healthy individuals were selected into 2 groups, including the young group: 17 individuals, aged 20 to 30 years old. Elderly group: 23 individuals, aged 65 to 75 years, were sleep-deprived for one month (data was obtained from the OpenfMRI website). Using the SPM12 Toolbox, preprocessing was performed to remove artifacts and noise. Then, ICA processing was done using the Gift toolbox in young and old people using fMRI data, and correlations between clinical variables and imaging were performed to extract insomnia biomarkers.

Results: In the Dynamic Range variable, the difference in the effect of insomnia between the two groups was significant in areas such as the Inferior Occipital Gyrus (IOG), Superior Temporal Gyrus (STG), and Posterior Cingulate (PC). The fractional amplitude of low-frequency fluctuations (fALFF) variable in the Anterior Cingulate and Precuneus areas, as well as the Spatial Maps variable in areas such as the inferior semilunar lobule, anterior cingulate, subcallosal gyrus, and middle temporal gyrus between the two groups, has a significant difference ($p=0.05$). Also, the fALFF variable in the anterior cingulate cortex and precuneus areas and culmen of Vermis had a significant difference in the two groups ($P<0.05$).

Conclusion: Based on the results of this study, it was shown that the brain activity map in sleep-deprived people has a significant change in some brain areas and this effect is different in old and young adults.

Keywords: Magnetic Resonance Imaging; Sleep Deprivation; Image Processing; Computer Assisted; Biomarkers.



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Investigate Effects of Music Therapy on Functional Connectivity in Papez Circuit of Breast Cancer Patients Using fMRI

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Abstract

Background: Despite the high prevalence of depressive symptoms in breast cancer survivors, they are often not diagnosed or treated in the health care system.

The aim of this study is to investigate activity and functional connectivity (FC) of Papez circuit networks associated with music processing using functional magnetic resonance imaging (fMRI) in depressed breast cancer patients.

Materials and Methods: Twenty-three breast cancer patients listened to four different Iranian/Persian music paradigms during the resting-state fMRI scanning session: negative stimulation of traditional music, negative stimulation of pop music, positive stimulation of traditional music and positive stimulation of pop music. The amplitude of low-frequency fluctuation (ALFF) was used to evaluate the local characteristics of spontaneous brain activity. FC maps were created using multivariate ROI-to-ROI connectivity (mRRC) and Papez circuit-based regions of interest (ROIs) selection. Provide a description of the research design, data collection and analysis.

Results: We found that music increases FC within various brain networks which are involved in memory, emotion, and cognitive function, including the limbic system, the default mode network (DMN), salience network (SN), and central executive network (CEN). Moreover, it seems that the traditional types (both positive and negative) of Iranian music may be more effective to affect brain activity in the patients with breast cancer, than the Iranian pop music.

Conclusion: These findings demonstrate that music therapy, as an effective and easily applicable approach, supports the neuropsychological recovery and can contribute to standard treatment protocols in patients with breast cancer.

Keywords: Breast Cancer; Music Therapy; Papez Circuit; Depression; Functional Connectivity.



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Bystander Effect of Sonodynamic Therapy on The Melanoma Cells

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Abstract

Background: In the bystander effect, non-irradiated cells receive biological signals from adjacent irradiated cells and undergo a variety of alterations, considered recently in non-ionizing irradiation like ultrasound waves.

This study was conducted to assess this effect on simultaneous administration of ultrasound and gold nanoparticles as a sonodynamic therapy which is an important newly stimuli-responsive method in cancer treatment.

Materials and Methods: Firstly, the appropriate concentration of Gold Nanoparticles (GNPs) and ultrasound intensity for sonodynamic therapy on melanoma cancer cells (A375) were evaluated. After treatments, the target cell culture was transferred to the bystander cells and the induced bystander effects including cell viability, apoptosis, expression of P53 (a promoter of apoptosis gene) and HO-1 (an inhibitor of apoptosis gene) were examined.

Results: According to the MTT results, 50 µg/ml concentration of GNPs and 1.5 W/cm² intensity of ultrasound wave were selected. Our results revealed that sonodynamic therapy induced bystander effect can alter the cell viability and apoptosis up to 20% and 51.61%, respectively. Moreover, a 2.9-fold increase in P53 gene expression and a decrease in HO-1 gene expression to 0.181-fold in comparison to the control groups were observed.

Conclusion: These results confirmed that bystander effect of sonodynamic can reduce the cancerous cell viability. Our finding showed that this treatment can potentially be an alternative to traditional treatment modalities.

Keywords: Bystander Effect; Sonodynamic Therapy; Gold Nanoparticles; Apoptosis; P53 & HO-1 Genes.



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Enhancement of the Blood-Brain Barrier Permeability due to Interaction of Focused Ultrasound and Nano-Bubbles –In Vitro Sonoporation

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Abstract

Background: By combining focused ultrasound application with nano-bubble system, we assume to induce the permeability of biological barriers and so, allowing drugs to enter the targeted part of a tissue. This occurs when nano-bubbles exert mechanical stresses on the cell membrane by oscillating. So far, the long ultrasound pulses have been employed regarding some preclinical and clinical cases. The purpose of this study is to optimize in vitro sonoporation through characterization of the effects of nano-bubble on tissue permeabilization rate. After fabrication and characterization of 100 nm lipid nano-bubbles, their effects under therapeutic ultrasound on sonoporation in the cells, utilizing Curcumin as fluorophore marker are verified.

Materials and Methods: First, nanobubbles containing curcumin were prepared and the size, surface charge, structure and constituent elements of the nanosystem were investigated using DLS, and TEM. Their dimensions were around 100 nm, with a dispersion coefficient of less than 0.3 and a surface charge close to neutral, with uniform spherical shapes and containing curcumin and SF₆ gas. TEM images showed that nanobubble containing curcumin is spherical with uniform size distribution. The morphology of curcumin-containing nanobubbles is presented by TEM images. We applied ultrasound pulses (according 1 MHz for central frequency, 10% duty cycle, 4.0 W/cm² as the intensity at 100 Hz pulse repetition frequency, 0.5 Seconds) onto the cells. Nano-bubbles containing Curcumin, as a drug model, was administered before application of ultrasound pulses. Cells were extracted after 6 hours of the ultrasound treatment to assess the extent of Curcumin. Triton X-100 (TX100) was used during an experimental period of 30 minutes. The cells underwent irreversible permeabilization of the membrane and structural collapse. The permeability of cell could determine with the aid of the scan methods in High Performance Liquid Chromatography (HPLC).

Results: HPLC of sonoporated cells showed obvious internalization of the Curcumin. The control sample, which was exposed to nano-bubbles and Curcumin without insonation, showed little or no residual Curcumin in the cells. Fluorescence intensity of sonoporated cells was statistically different from those unsonoporated with bubbles at at the same concentration, also the fluorescence intensity of cells sonoporated with the bubbles was statistically different with the same concentration of Curcumin.

Conclusion: The results of this study indicate that nano-bubble can interact dynamically to affect sonoporation efficiency. With respect to the role of nano-bubbles for sonoporation of adherent cells, the additional control over drug-delivery and improvement in drug-uptake is promising.

Keywords: Blood Brain Barrier; Drug Delivery; High Intensity Focused Ultrasound; Nano Bubbles.



Concept Evaluating of Image Reconstruction Algorithms SSRB and FORE in the Brain CT

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Abstract

Background: A study by Kinahan *et al.* found Fourier Rebinning (FORE) to have favorable trade-offs between speed and accuracy over 3D Reprojection (3DRP) for rapid CT reconstruction. FORE demonstrated significantly higher peak signal-to-noise ratio and lower mean squared error compared to 3DRP, indicating lower noise and higher fidelity. The authors attributed this performance to FORE better preserving spatial resolution properties versus 3DRP's reprojection model.

The objective of this study is to conduct a quantitative and qualitative evaluation of two image reconstruction algorithms, FORE (Fourier Rebinning) and SSRB (Single Slice Rebinning), using brain Computed Tomography scan (CT scan) images. To quantitatively assess the outputs of the two reconstruction algorithms, four comparison metrics were utilized: mean squared error (MSE), Peak Signal-to-Noise Ratio (PSNR), Structural similarity Index (SSIM), and Contrast-to-Noise Ratio (CNR). Furthermore, the qualitative evaluation of the network detection was performed using the Receiver Operating Characteristic (ROC) curve. The ROC curve is a graphical representation of the trade-off between the true positive rate and the false positive rate. It provides a comprehensive assessment of the algorithm's sensitivity and specificity in detecting network features.

Materials and Methods: Fourier Rebinning (FORE) and Single Slice Rebinning (SSRB) are algorithms used to reorganize scan data into a stack of 2D sinograms prior to image reconstruction. FORE applies a Fourier transform to the reorganized parallel projections. This is more computationally intensive than SSRB but can provide improved image quality since it models the data in the Fourier domain. SSRB simply recombines projection data into fewer angles and reconstructs each 2D slice with back-projection. It is faster than FORE as it does not require interpolation or Fourier transforms. However, it can introduce more noise and artifacts compared to FORE since it does not model the data in Fourier space.

Results: The results of the quantitative evaluation using MSE, PSNR, SSIM, and CNR will be presented and compared for the FORE and SSRB algorithms. Additionally, the ROC curves will be plotted to visualize and compare the qualitative performance of the algorithms in network detection.

Conclusion: The findings from the comparison parameters clearly demonstrated the superior performance of the FORE reconstruction algorithm over the SSRB reconstruction algorithm. In addition, using a convolutional neural network model, we carefully created ROC curves for both algorithms, which allows us to obtain the area under the ROC Curves (AUC) for each algorithm. These results not only solidify the efficacy of the FORE reconstruction algorithm but also emphasize the prowess of our chosen computational approach. These results will contribute to the optimization and selection of image reconstruction algorithms in brain CT imaging, ultimately enhancing the diagnostic accuracy and quality of patient care.

Keywords: Computed Tomography Scan; Fourier Rebinning; Reconstruction Algorithm; Receiver Operating Characteristic Curve; Single Slice Rebinning.



Determination of Polyphenols in GC- MS Analysis and Antioxidant Activity of Propolis Ethanolic Extract as a Linker in Nanofibers

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Abstract

Background: Polyphenols are typically used as micronutrients. In addition, due to their significant roles, they have gained considerable interest in the field of biomaterials. One potential source of polyphenols for use in biomaterials is the ethanolic Extract of Propolis (EP). Propolis is a natural resin produced by honey bees, and its extract exhibits strong antimicrobial, anti-inflammatory, and antioxidant activities. Polyphenols in EP serve as potent antioxidants and can also function effectively as natural binders. The geographical origin, extraction method, and extraction conditions of the extract can influence the polyphenol content and the structure of polyphenolic compounds within the ethanolic extract of propolis. In this research, Mass Spectrometry (GC-MS) was employed to analyze propolis ethanolic extract, aiming to determine its geographical origin and assess its antioxidant content through the DPPH assay. Additionally, electrospun fibers were fabricated using PVA incorporated with EP, while the intermolecular interactions between the matrix and the extract were examined. The presence of EP in the fibers was evaluated using Infrared Spectroscopy (FTIR) and Scanning Electron Microscopy (SEM) microscopy.

Materials and Methods: To determine the work methodology, it is crucial to acknowledge that the extraction method significantly influences the quantity and composition of the resulting compounds. In this study, extraction was conducted using 70% alcohol with continuous agitation for 48 hours at 37 degrees Celsius. To enhance the extraction process and prevent thermal degradation, ultrasonic waves were applied for 10 seconds, followed by concentration of the obtained extract via rotary evaporation. Compound analysis was carried out using GC-MS, and the assessment of antioxidant activity was performed using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) method. We fabricated the desired scaffolds, incorporating specific concentrations of PVA and EP, through the electrospinning technique. Finally, we analyzed the chemical structure and thermal stability using FTIR and examined the constituents' interaction through SEM.

Results: The GC-MS analysis of EP identified multiple compounds in the propolis ethanolic extract, such as hydroxycinnamic acid and coumaric acid. Furthermore, the analysis revealed the presence of flavonoids, esters, and terpenes in EP. Structural analysis of the scaffolds indicated that fibers enriched with phenolic compounds from propolis create a more homogeneous and suitable matrix. The investigation of DPPH confirmed that the biological activity and efficacy of the electrospun fibers are linked to the unique chemical composition of propolis and its antioxidant activity.

Conclusion: The results of this research demonstrate the suitability of propolis extract for biomaterial applications, attributed to its beneficial polyphenolic compounds with antioxidant properties. Structural analysis revealed that the incorporation of polyphenols from propolis extract into the electrospun matrix of polyvinyl alcohol improved fiber stability, acting as a natural linker. This dual role of polyphenols not only enhances antioxidant and anti-inflammatory attributes but also reinforces the fiber structure.

Keywords: Propolis Ethanolic Extract; Mass Spectrometry; Polyphenol; Antioxidant.



Intelligent Scleroderma Diagnosis Method by Skin Tissue Image Analysis and Deep Learning

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Abstract

Background: Skin diseases can result from fungal growth on the skin, hidden bacteria, allergic reactions, or pigment. Chronic skin diseases are persistent conditions and can sometimes transform into malignant tissues. Scleroderma, recognized as an autoimmune rheumatic disease or a connective tissue disorder, causes skin thickening and dryness and occasionally causes swelling in the limbs. Vascular disorders can lead to non-healing ulcers, gangrene, and finger amputation in this condition. Scleroderma patients may also experience heart failure and pulmonary hypertension. In addition, the accumulation of fibers and other collagens impairs joints in the hands, feet, lungs, kidneys, and the gastrointestinal system, particularly the esophagus, leading to disability. Consequently, early and precise diagnosis is essential, yet challenges persist due to limited specialists and misdiagnoses, emphasizing the urgent need for accurate detection.

Developing an intelligent diagnosis system to identify scleroderma from healthy skin and providing intelligent therapeutic solutions and necessary steps to increase the likelihood of the patient's recovery.

Materials and Methods: 45 samples from scleroderma patients and 14 healthy samples, all previously surgically prepared and stored as separate blocks in the Razi Skin Hospital's laboratory bank, were obtained. After defreezing, these samples were sectioned into three thicknesses using a microtome and mounted on microscope slides. In the biophotonics laboratory, imaging and dataset creation were performed using OPTIKA microscopy and specialized software. As a result, 596 images from scleroderma-affected skin and 477 images from healthy skin were collected using samples. Subsequently, preprocessing tasks, including size adjustment, lighting correction, resolution standardization, and noise reduction, were applied to the collected images to analyze and prepare them for model training.

Results: Our intelligent diagnosis system achieved an accuracy close to 85% in identifying scleroderma and healthy skin through image analysis. Additionally, preprocessing the images in our dataset standardized the dataset for use by artificial intelligence algorithms, enabling versatile applications for various research purposes and yielding valuable outcomes.

Conclusion: Our study aimed to improve the outcomes for individuals affected by scleroderma. Utilizing deep learning, convolutional neural networks, and image analysis, we sought to enhance diagnosis accuracy and minimize errors associated with this condition. By employing these advanced techniques, our research contributes significantly to supporting affected individuals, especially in regions with limited access to specialized medical professionals.

Keywords: Scleroderma; Diagnosis System; Image Analysis; Deep Learning.



Microbubble and Ultrasound Assisted Photodynamic Therapy of Breast Adenocarcinoma

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Abstract

Background: Breast cancer is one of the most common cancers in women, which has increased dramatically in recent years. One of the treatment methods for this disease is photodynamic therapy. Research shows that a photosensitizer, encapsulated in a nanoliposome, increases therapeutic efficiency. In addition, microbubble collapse has been widely used for drug and gene transfer. Vibration and contact of bubbles with the cell membrane accelerate the transfer of particles.

In this research, albumin microbubbles with ultrasound are used to increase drug uptake of Methylene blue by tumor cells, and the effect of ultrasound repetition in the presence of microbubbles has been investigated.

Materials and Methods: The research was conducted in 9 groups of 5 Balb/c mice and the effectiveness of sonophotodynamic therapy in the presence of methylene blue and albumin microbubbles and the absence of albumin microbubbles were investigated.

Results: In the presence of albumin microbubble and ultrasound, photodynamic therapy induced a significant decrease in the tumor growth process compared to other groups ($P < 0.05$). Also, there was a significant difference between the time of doubling, five-fold, and seven-fold tumor volume in the treatment group compared to the control and sham groups. In addition, the survival time of the animals in this group was significantly different from other groups ($P < 0.05$).

Conclusion: The effectiveness of treatment of photodynamic therapy in the presence of albumin microbubble and ultrasound was higher than other treatment groups.

Keywords: Microbubble; Methylene Blue; Adenocarcinoma; Sono Photodynamic Therapy; Ultrasound Waves.



In Vivo Molecular Imaging in Short Wave Infrared Region of Spectrum Using One-Dimensional Nanostructures for Cell Tracking

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Abstract

Background: Labelling and observation of infused cell fate and engraftment using traditional imaging modalities is limited due to some limitations such as the false positive results and short half-life of radio-tracers in Magnetic Resonance Imaging (MRI) and nuclear medicine, respectively. Also, tracking of transplanted cell dynamic behaviour using bioluminescent imaging due to the mutational risk is worrying.

Cellular imaging using one-dimensional nanostructures fluorophores is expected to contribute to the progression of regenerative medicine, due to their well-known characteristics such as emitting in the extended region of the electromagnetic spectrum.

Materials and Methods: Fluorescence imaging of transplanted cells labelled with one-dimensional nanostructures in the short-wave infrared region of the spectrum could offer better temporal and spatial resolution due to a decrease in photon scattering, tissue absorption, and autofluorescence.

Results: One-dimensional nanostructured fluorophores hold great promise for the real-time and non-invasive visualization of stem cell engraftment, fate, and cellular dynamics in a living body with outstanding spatial and temporal resolution.

Conclusion: While each imaging technique has its own limitation for cell tracing, in vivo molecular imaging in the short-wave infrared region of the spectrum has opened new ways for advanced regenerative therapy.

Keywords: Short Wave Infrared; In Vivo Molecular Imaging; Cell Tracking; Fluorescence Imaging.



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Tracking of Exosomes Encapsulated in an Injectable Hydrogel Using in Vivo Molecular Imaging

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Abstract

Background: Exosome transplantation is one of the most promising strategies for the minimally invasive delivery of bioactive molecules to injured tissue. However, an important challenge to its efficacy is poor uptake by target tissue due to a lack of mechanical protection during injection and an unfavourable microenvironment of living body. Exosome uptake by the mononuclear phagocyte system and rapid clearance from body known as some important obstacles for successful treatment of various tissue by these bioactive entities.

Encapsulation of exosome in conductive hydrogel enable their controlled release and maintenance of their efficacy.

Materials and Methods: Injectable hydrogel offers many advantages including an appropriate degradation rate, low immunogenicity reduced risk of mutation and carcinogenicity.

Molecular imaging and tracking of transplanted exosomes labelled with various contrast agents could offer better understanding of their fate.

Results: Molecular imaging results demonstrate that encapsulation of exosome in hydrogel enable their controlled release and maintenance of their efficacy.

Conclusion: Molecular imaging holds great promise for the real-time and non-invasive visualization of encapsulated exosomes fate and dynamics in a living body with outstanding spatial and temporal resolution.

Keywords: Exosome; In Vivo Molecular Imaging Tracking; Encapsulation; Hydrogel.



6th International TPCF Preclinical Imaging Symposium



Improvement of Breast Tumor Imaging by Multifunctional SPION Nanoparticles Conjugated with a Novel Engineered Endostatin Peptide

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Abstract

Background: Superparamagnetic Iron Oxide nanoparticles (SPIONs) have emerged as valuable tools in cancer studies and imaging. Their magnetic properties make them ideal candidates for Magnetic Resonance Imaging (MRI) contrast agents. SPIONs offer enhanced imaging capabilities, enabling researchers to visualize and track cancer cells with precision. Additionally, when surface-modified with specific ligands or peptides, SPIONs can be tailored for targeted cancer cell imaging. This versatility has revolutionized preclinical cancer research, allowing for non-invasive, high-resolution imaging of tumors and aiding in the development of novel diagnostic and therapeutic strategies.

Materials and Methods: The primary aim of our research was to design a multifunctional nanoparticle with Superparamagnetic Iron Oxide (SPION), coated with Diethylenetriaminepentaacetic Acid (DTPA) to reduce SPION toxicity. This innovative nanoparticle was engineered to bear carboxylic groups and was subsequently conjugated with an endostatin peptide, which specifically binds tumor cells and tumor endothelial cells, to achieve targeted imaging in 4T1 mammary carcinoma tumor model.

Results: The results of our study confirmed the successful design and synthesis of the multifunctional nanoparticles, highlighting their promising properties. The FTIR analysis demonstrated that the synthesis, DTPA coating, and peptide targeting occurred as intended. Importantly, the MRI images of mice bearing xenograft breast cancer revealed the nanoparticles' remarkable ability to target and image tumor cells, owing to their conjugation with endostatin peptides.

Conclusion: In conclusion, the multifunctional nanoparticles described in this study represent a significant advancement in preclinical research. Their unique combination of SPION core, DTPA coating, and endostatin peptide targeting offers a powerful tool for non-invasive, targeted cancer cell imaging. These nanoparticles have the potential to revolutionize preclinical imaging studies and enhance our understanding of cancer biology.

Keywords: Superparamagnetic Iron Oxide Nanoparticles; Cancer Imaging; Tumor Targeting; Magnetic Resonance Imaging.



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Microvascular Three-Dimensional Imaging of Tumors

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Abstract

Background: Recent development of cancer treatments, scientists have realized the effect of vasculature in choosing the treatment method and drug delivery to the tumor tissue. Therefore, they seek to develop accurate imaging methods of microvessels inside cancer tissues. To prepare such images, a X-ray micro-Computed Tomography (μ CT) and a suitable contrast agent are needed.

The aim of this research is to compare new techniques for 3D imaging of microvessels network inside cancer tissues.

Materials and Methods: By studying the scientific articles of the last two decades, proposed methods to obtain the desired images have been extracted. Advantages, disadvantages and limitations are discussed.

Results: Josef Ehling *et al.* (2014) show that the combination of functional in vivo and anatomical ex vivo μ CT allows highly accurate vessel size and vessel branching of blood volume and highly detailed three-dimensional analysis of the vascular network in tumors. This work has been examined in two types of cancer models (A431 & A549). Ruslan Hlushchuk *et al.* (2018) describe μ Angiofil-enhanced μ CT-based visualization of vasculature within different cancerous tissues. μ Angiofil is a new polymerizing contrast agent for microangiography imaging of entire vascular networks. The contrast agent homogeneously fills the entire vasculature and remains elastic enough for long term storage in 2% PFA. The additional autofluorescent properties of the contrast agent that allows for histological analysis and correlative microscopy.

Conclusion: μ CT with μ Angiofil is a new efficient tool to study physiological and pathological changes in microvessels inside tumors. This approach has enabled non-destructive 3D imaging of tumor tissue along with its vascular network. One of the disadvantages of this method is that it is performed on tissues outside the body.

Keywords: Microvascular; Angiogenesis; Three Dimensional; Tumor; Contrast Agent.



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^{99m}Tc-Dendrimer-Rituximab: New Contrast Agent for Lymph Node Imaging

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Abstract

Background: Dendrimer-Rituximab is a new contrast agent that bind to a specific part of B cells called the CD20 receptor. In this study we did a research to use this compound for finding sentinel lymph nodes in burn infection disease.

Materials and Methods: The dendrimer was synthesized utilizing citric acid and polyethylene glycol diacid as precursor and Dicyclohexyl Carbodiimide (DCC) crosslinker. Conjugation of rituximab was done by utilizing 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide/N-Hydroxysuccinimide (EDS/NHS) crosslinker between amine and acid groups. 3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide (MTT) examination was performed to assess biocompatibility and at last Magnetic Resonance Imaging (MRI) imaging was performed to look at the bio-distribution of the medicate within the in vivo environment.

Results: Tests showed that the bioconjugate was successfully made and. The toxicity test results showed that the desired compound is biocompatible with Human embryonic kidney 293 cells (HEK-293 cells). The Single-photon Emission Computed Tomography (SPECT) imaging indicate the ability of this compound for lymph node imagine.

Conclusion: Because dendrimers are compatible with the body, can dissolve in water, and are good at carrying ^{99m}Tc and binding to antibody, they have a good ability to be used for imaging without affecting how the antibody works in the body.

Keywords: Dendrimer; Rituximab; ^{99m}Tc; Lymph Node; Single Photon Emission Computed Tomography.



Imaging of Metastatic Breast Cancer Using Tumor Targeting Solid Lipid Nanoparticles

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Abstract

Background: The application of tumor-targeted ligands is a common strategy to improve the specificity cancer detection. In this study, superparamagnetic iron oxide (Fe₃O₄) was prepared as a negative contrast agent in Magnetic Resonance Imaging (MRI) and loaded into a Solid Lipid Nanoparticle (SLN). Then, a tumor-targeting peptide derived from human endostatin was conjugated to the surface of SLN.

The aim of this research is to synthesize and characterize a diagnostic nanoparticle to specifically target the murine 4T1 breast tumor model and enhance MRI contrast.

Materials and Methods: Fe₃O₄ was prepared using the coprecipitation method. SLN containing Fe₃O₄ were synthesized using the microemulsion technique. The peptide was covalently coupled to the carboxyl groups of SLN by its N-terminal. The *in vitro* characteristics of the nanoparticle were evaluated by Dynamic Light Scattering (DLS), zeta potential, Vibrating Sample Magnetometer (VSM), X-ray Diffraction (XRD), Fourier-transform Infrared Spectroscopy (FTIR) and Scanning Electron Microscope (SEM). The cytotoxicity of the nanoparticle was assayed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), and the tumor-targeting efficiency was measured by MRI *in vivo* and *ex vivo* histopathology.

Results: The results showed that the nanoparticle was successfully prepared. The nanoparticles' mean size was 315 nm, their Polydispersity Index (PDI) was 0.3, and peptide-uncoated nanoparticle showed more negative zeta potential than peptide-coated ones. VSM confirmed the magnetic property of Fe₃O₄. The crystal structure of Fe₃O₄ and its incorporation into SLN were confirmed by the XRD patterns. FTIR spectroscopy indicated the formation of peptide-coated Fe₃O₄-loaded SLN. SEM confirmed that nanoparticles are spherical and uniform. The cytotoxicity assay demonstrated that it had appropriate cytotoxicity for 4T1 and MCF7 cells. The targeting efficiency was confirmed via MRI of 4T1 tumor-bearing Balb/c mice. The histopathology data confirmed that, in contrast to controls (SLN containing Fe₃O₄), peptide-conjugated Fe₃O₄-loaded SLNs specifically accumulated in tumors.

Conclusion: We successfully developed peptide conjugated-magnetic SLNs that can be used for the detection of breast tumors through magnetic resonance molecular imaging.

Keywords: Tumor Targeted Peptide; Superparamagnetic Iron Oxide; Solid Lipid Nanoparticle; Magnetic Resonance Imaging.



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Effects of Sex, Fasting, and Anesthesia Agents on SUV_{mean} in FDG-PET Imaging of 4T1 Tumor-Bearing Mice: A Quantitative Evaluation during a 120-Minute Scan

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Abstract

Background: Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) imaging is a powerful tool for studying tumor metabolism in preclinical models. Understanding the temporal changes in FDG uptake is crucial for unraveling tumor behavior, optimizing experimental protocols, and enhancing data interpretation. Additionally, sex-related differences in glucose metabolism and fasting, as well as the choice of anesthesia agents, can influence FDG uptake. Evaluating these factors is important for accurate interpretation and comparability of preclinical tumor imaging studies.

This study aims to conduct a quantitative analysis of the changes in mean Standardized Uptake Values (SUV_{mean}) during the 120-minute FDG-PET imaging scan in 4T1 tumor-bearing mice. Specifically, we will evaluate the effects of sex, fasting, and the anesthesia agents on the FDG uptake dynamics within the tumor, brain and heart tissues. The significance of this evaluation lies in its potential to optimize experimental protocols and enhance the accuracy of data interpretation in cancer research and therapy development.

Materials and Methods: In this study, we investigated the impact of various parameters on FDG-PET scan outcomes using female and male BALB/c mice bearing 4T1 cell xenografts. To assess the effects of fasting, both male and female mice were divided into two groups: those subjected to 24 hours of fasting and non-fasted mice. Additionally, we compared the use of two anesthesia agents, ketamine-xylazine combination and isoflurane, to evaluate their influence on SUV_{mean}. Imaging was conducted immediately after administration of 12 MBq of FDG, with imaging intervals of 15 minutes and continued for 120 minutes post-injection. Manual delineation of Regions of Interest (ROIs) was performed around the tissues of interest, and quantitative parameters were calculated based on these ROIs.

Results: The results indicate that non-fasted female mice had higher tumor SUV_{mean} compared to male mice throughout the 120-minute experiment. SUV_{mean} remained constant in tumor tissue for non-fasted male mice. Fasting resulted in an increase in tumor and brain SUV_{mean} for male mice, peaking at 30 minutes. No significant difference in SUV_{mean} was observed between non-fasted female and male mice groups in the brain. Additionally, the ketamine-xylazine group had higher SUV_{mean} values than the isoflurane group in tumor tissue and brain. In the heart tissue, SUV_{mean} values remained constant in the isoflurane group but decreased significantly in the ketamine-xylazine group.

Conclusion: Fasting led to notable changes in tumor and brain SUV_{mean} in male mice, suggesting a sex-specific metabolic response to fasting. Ketamine-xylazine anesthesia resulted in higher SUV_{mean} values in tumor tissue and brain compared to isoflurane anesthesia. These findings highlight the need for optimized imaging protocols to ensure accurate assessment of metabolic activity in different tissues.

Keywords: Fluorodeoxyglucose-Positron Emission Tomography; 4T1 Tumor; Anesthesia; Fasting; Standardized Uptake Values.



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Quantitative Analysis of Radionuclide Distribution Alterations in Mice Induced by Music Exposure During FDG-PET Scan

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Abstract

Background: The therapeutic use of music is gaining popularity, showcasing significant effects on various biological systems. Preclinical studies have found valuable insights into the metabolic effects of music interventions through the use of Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET). Nonetheless, it is imperative to establish baseline data on the distribution of FDG in laboratory animals' bodies in order to accurately assess the effects of music interventions on them. This foundational information is vital for the precise interpretation and evaluation of the metabolic alterations induced by music interventions.

In this study, we aimed to investigate the impact of music on FDG uptake in BALB/c mice bearing 4T1 tumors using PET scan imaging. By examining the effects of music on FDG uptake in the body, we sought to provide valuable insights into the potential influence of music interventions.

Materials and Methods: Female BALB/c 4T1 tumor-bearing mice, were allocated randomly into music group and the control group. The mice in the music group were exposed to Mozart's music for a duration of 30 minutes prior to the administration of the radiopharmaceutical injection, as well as during anesthesia and radionuclide uptake. On the other hand, the control group underwent imaging in a silent environment under normal conditions. FDG-PET scan conducted 60 min post-injection. To analyze the data, manual delineation of Regions Of Interest (ROIs) surrounding the relevant tissues was performed, and quantitative parameters were then calculated based on these ROIs.

Results: The findings indicated that the use of music did not result in a significant change in the range of tumor mean standardized uptake value (SUV_{mean}). However, when compared to the group exposed to silence, the music group exhibited a slight increase in brain SUV_{mean} and brain percentage of injected dose per gram (%ID/gr) in the ex vivo analysis, which was nearly double. Conversely, the SUV_{mean} and %ID/gr of the heart in the ex vivo experiments were approximately half that of the silence group. The measurements of blood activity demonstrated a significant decrease in the music group, and a similar decreasing trend was observed in muscle SUV_{mean} following exposure to music.

Conclusion: Fasting led to notable changes in tumor and brain SUV_{mean} in male mice, suggesting a sex-specific metabolic response to fasting. Ketamine-xylazine anesthesia resulted in higher SUV_{mean} values in tumor tissue and brain compared to isoflurane anesthesia. These findings highlight the need for optimized imaging protocols to ensure accurate assessment of metabolic activity in different tissues.

Keywords: Fluorodeoxyglucose-Positron Emission Tomography; Positron Emission Tomography; Mice; 4T1 Tumor.



Comparative Effective Dose of ^{68}Ga -EDTA, $^{99\text{m}}\text{Tc}$ -DMSA, and $^{99\text{m}}\text{Tc}$ -DTPA in Renal Scans of The One-Year-Old Paediatric Using Reference Voxel Phantoms

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Abstract

Background: Due to the fact that paediatric are more sensitive to the effects of radiation than adults, however, the evaluation of paediatric radiation dose has received less attention. Renal scintigraphy plays an important role in diagnosing various kidney disorders. This procedure can be done with different radiopharmaceuticals. Patients undergoing renal Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT) scan will receive a radiation dose that must be evaluated.

^{68}Ga -EDTA, $^{99\text{m}}\text{Tc}$ -DMSA, and $^{99\text{m}}\text{Tc}$ -DTPA are radiopharmaceuticals that are commonly used to evaluate renal function by PET and SPECT scans. In this study, the effective doses caused by these radiopharmaceuticals were calculated in one-year-old paediatric.

Materials and Methods: By studying the scientific articles of the last two decades, proposed methods to obtain the desired images have been extracted. Advantages, disadvantages and limitations are discussed.

Results: The results show that the highest effective dose per unit activity administered is due to ^{68}Ga -EDTA ($1.6\text{E}-01 \text{ mSv.MBq}^{-1}$) and $^{99\text{m}}\text{Tc}$ -DMSA ($2.2\text{E}-02 \text{ mSv.MBq}^{-1}$) and $^{99\text{m}}\text{Tc}$ -DTPA ($1.0\text{E}-02 \text{ mSv.MBq}^{-1}$) are in the next order, respectively. The absorbed dose of the bladder wall for ^{68}Ga -EDTA, $^{99\text{m}}\text{Tc}$ -DTPA, and the kidneys for $^{99\text{m}}\text{Tc}$ -DMSA have the largest contribution to the effective dose.

Conclusion: Using new one-year-old paediatric reference voxel phantoms (ICRP143) could provide a better estimate of organs absorbed doses and whole-body effective doses due to its realistic structure. $^{99\text{m}}\text{Tc}$ -DTPA can be a better option than other studied radiopharmaceuticals due to its lower effective dose per unit activity administered. The absorbed dose to the kidneys and bladder wall is often one of the doses that limit the activity administered. Therefore, the results obtained in this research may be useful to evaluate the injected activity.

Keywords: Effective Dose; Paediatric Voxel Phantoms; GATE.



Comparing the Imaging Quality of Head and Neck Computed Tomography Scans in Cannon and General Electric CT Scanners

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Abstract

Background: Today, various modalities are used in diagnostic imaging, the most important of which is Computed Tomography (CT) scan. CT scan exams have increased in the recent years depending on the various factors, including the corona virus. According to recent studies, to evaluate the brain in terms of injuries, lesions, intracranial bleeding, and tumors, head and neck CT scan, is the preferred selective diagnostic imaging method.

The use of different CT scan devices can affect the quality of the images taken from the head and neck region according to the device conditions such as detectors type, imaging protocol, software and image reconstruction algorithm. Each of the image areas directly or indirectly affects the final image that is sent to the physician for diagnosis. The aim in this study is to compare the images of two different CT scanners in terms of the image quality of head and neck CT scans under the same radiation conditions for each area.

Materials and Methods: In this study, Cannon and General Electric (GE) CT scanners and PMMA phantoms were used to record phantom images which was placed in the isocenter of the device and was irradiated in the same imaging protocol (120 kV, 150 mAs). Iterative Reconstruction (IR) algorithm and Adaptive Statistical Iterative Reconstruction (ASIR) algorithm were used for Cannon CT scan and GE CT scan, respectively. Four slices were selected in the same way and set with the same window width and window level from the CT-gram images. Software of ImageJ, checking ROIs in similar places used for image analysis. Also, image noise values were compared in two devices.

Results: Ten Region of Interest (ROI) were taken from each CT grams of the head and neck CT scan (two at 12 o'clock, two at 3 o'clock, two at 6 o'clock, two at 9 o'clock and two at the center with an area of 25 mm²) and the study was done on the determined CT-grams. The average CT numbers in Cannon and GE devices were 180 and 175 Hounsfield, respectively. The average noise values were equal to 8 and 2.5 respectively.

Conclusion: The comparison of the data related to the images has shown that there is a significant difference between the image quality recorded from the two devices in terms of image noise, as well as the images obtained from GE had lesser noise values.

Keywords: Image Noise; Computed Tomography Number; Head and Neck Computed Tomography.



The Effect of Attenuation Correction on Image Uniformity of Xtrim_PET: A Monte Carlo Simulation Study

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Abstract

Background: Preclinical Positron Emission Tomography (PET) scanners are widely used to focus on transitional research from preclinical study to human clinical applications. So, small animal PET imaging is increasingly used for validation of radiotracers to use in human. For this purpose, increasing accuracy of image quantification is very important.

Attenuation coincidences can cause underestimation of tracer uptake in organs, so attenuation correction is a main factor in quantification of the PET images. Hence, the aim of this study is evaluation of the effect of attenuation correction on image quantification of preclinical Xtrim_PET scanner.

Materials and Methods: Monte Carlo simulation of Xtrim_PET scanner was performed using GATE (V9.1). This scanner composed of 10 detector blocks and each block consists of 24×24 arrays of 2×2×10 mm³ LYSO scintillator. Energy window of 350 keV to 650 keV was selected and adjusted for data acquisition. To evaluate the effect of attenuation correction on uniformity, a uniform cylindrical phantom with diameter of 90 mm filled with 200 μCi 18F-FDG, was simulated. Attenuation correction was done using Chang method. Chang's method is a non-transmission attenuation correction method in uniform regions in PET and SPECT imaging systems. In this method, the image was first reconstructed and then contoured using Otsu's thresholding method. Then, the soft tissue attenuation coefficient at 511keV -based on ICRU 44- was assigned to the contoured area and the attenuation correction factor was calculated. The attenuation corrected image was reconstructed with attenuation weighted OSEM algorithm (4it, 4sub) via in-house software. Uniformity was calculated based on NEMA NU-4 procedure.

Results: Coefficient of Variation (COV) of simulated uniform phantom decreased from 50% to 41% after implementation of attenuation correction. The count profile of non-attenuation corrected image illustrated increased counts at the periphery compared to the center, but in the attenuation corrected image the count of center increased and led to an increase in image uniformity.

Conclusion: It should be noticed, that the Xtrim_PET scanner is not equipped with Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) imaging modalities, Chang's method, which is an attenuation correction method without the need to use CT and MRI images, can be used to increase the quantitative and qualitative quality of the reconstructed images.

Keywords: Positron Emission Tomography; Preclinical; Attenuation Correction; Quantification.



Evaluation of Tail Fitting Scatter Correction on Image Quantification of Xtrim_PET: A Simulation Study

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Abstract

Background: Today small animal Positron Emission Tomography (PET) imaging has widely been used to quantitative assessment of metabolic evaluation of cellular biology and development of new pharmaceuticals. But scatter coincidences are one of the importance factors can lead to incorrect estimation of tracer uptake in animal organs.

Due to the importance of scatter coincidences on image quantification, the purpose of the present study is to evaluate the importance of scatter correction on reconstructed image of preclinical Xtrim_PET scanner.

Materials and Methods: Monte Carlo simulation of Xtrim_PET scanner was performed using GATE (V9.1). This scanner composed of 10 detector blocks and each block consists of 24×24 array of 2×2×10 mm³ LYSO scintillators. To evaluate the effect of scatter correction, an image quality phantom was used. This phantom consists of three main parts: 1) two cold chambers filled with water and air to calculate spilled over ratio (SOR), 2) uniform region to uniformity evaluation and 3) five fillable rods (diameters: 1, 2 3 4 and 5 mm) to evaluate the recovery coefficient (RC). The phantom was filled with 3.7 MBq 18F-FDG. Scatter correction was done using tail fitting method. In this method the object boundaries were determined from non-corrected image. Then a 1-D gaussian is fitted to the projection tails in each projection angle to obtain scatter component. Scatter corrected sinogram was obtained using subtraction of the estimated scatter components from measured projections. The scatter corrected image was reconstructed with attenuation weighted OSEM algorithm (4it, 4sub) using an in-house software. SOR was calculated based on NEMA NU-4 procedure.

Results: Results showed that applying scattered correction led to decrease in SORs by 10% and 15% in water and air-filled chambers, respectively. Also, the linear profile in the middle slice of uniform region of the image quality phantom showed that this method has been able to correct the out of field of view activity.

Conclusion: The tail fitting method is a fast and simple method to scatter correction in projection space and it mostly used to correct out of field of view scatter coincidences. This method can lead to an increase in image quantification accuracy in preclinical studies.

Keywords: Positron Emission Tomography; Preclinical; Scatter Correction; Quantification.



Quantitative Ultrasound Radiomics for Early Detection of Liver Fibrosis: A Preclinical Review

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Abstract

Background: Liver fibrosis is characterized by the excessive deposition of extracellular matrix and can progress irreversibly into cirrhosis if not treated well or discovered timely. Cirrhosis accounts for 2 million deaths worldwide yearly. Early detection of liver fibrosis is therefore essential for better patient management. Currently, biopsy is the gold standard for diagnosing liver fibrosis and assessing disease severity. However, its application is limited due to invasiveness, unrepeatability, high sampling errors, and different interpretations. Radiomics is a specific method of extracting and analyzing high-dimensional quantitative imaging features. Radiomics features include tissue intensity, shape, texture, and advanced statistical properties, which are mostly imperceptible by eye. Ultrasound radiomics enables the non-invasive, safe, and effective detection of liver fibrosis.

In this review, we aim to emphasize key findings from previous preclinical studies and broaden the potential applications of quantitative ultrasound radiomics for early detection of liver fibrosis.

Materials and Methods: This study was conducted as a comprehensive review by searching multiple information databases, including PubMed, Embase, ProQuest, and Web of Science, covering the period from 2018 to 2023. Articles that cited related studies were also searched to find any related publication (using PubMed, and Google Scholar citation tracking tools).

Results: Most of the features extracted from rat liver ultrasound images, including first-order histogram, Run Length (RL), and Gray Level Co-occurrence Matrix (GLCM), showed a significant difference between the advanced and early liver fibrosis. The most significant differences observed were in echo-intensity and heterogeneity which were higher in advanced vs early fibrosis. The performance of the individual ultrasound features in detecting early and advanced liver fibrosis showed high sensitivity and specificity and led to the best classification.

Conclusion: Quantitative ultrasound radiomics can serve as a precise and non-invasive tool for assessing fibrosis, with the potential to detect fibrosis changes and differentiate between early and advanced liver fibrosis. Future research can further improve the sensitivity of quantitative ultrasound in evaluating liver fibrosis without requiring biopsies, thereby addressing the limitations of ultrasound in detecting early-stage fibrosis.

Keywords: Preclinical; Liver Fibrosis; Radiomics; Quantitative Ultrasound.



Potential of Proton Magnetic Resonance Spectroscopy in Breast Cancer Diagnosis MRS in Breast Cancer

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Abstract

Background: Despite the progress made in therapy, the timely detection of breast cancer remains essential in order to achieve improved patient outcomes and reduced mortality rates. The advancements in metabolite and metabolic activity detection technologies have reached a level of sophistication that enables their use in the investigation of cancer metabolism. Proton Magnetic Resonance Spectroscopy (MRS), a non-invasive diagnostic method, has significant potential for examining breast cancer metabolism. After performing contrast-enhanced Magnetic Resonance Imaging (MRI), spectroscopic imaging data may be obtained from the Magnetic Resonance (MR) voxel containing the breast lesion using either the Point Resolve Spectroscopy Sequence (PRESS) or the Stimulated Echo Acquisition Mode (STEAM) sequence. Multiple Nuclear Magnetic Resonance (NMR) investigations using ¹H and ³¹P MRS nuclei, conducted in vivo, in vitro, and ex vivo, have shown compelling evidence of modified choline and phospholipid metabolism in human breast cancer tissues. Extensive research has been conducted on the use of Magnetic Resonance Spectroscopy (MRS) as a supplementary tool to morphologic and dynamic MRI with the purpose of enhancing diagnostic accuracy in breast cancer and reducing the occurrence of unnecessary benign biopsies.

The objective of this study is to conduct a comprehensive analysis in order to assess the diagnostic efficacy of breast proton MR spectroscopy in distinguishing between benign and malignant lesions. Additionally, this review aims to identify the factors that have an impact on the accuracy of MRS.

Materials and Methods: The study extensively evaluated the existing literature using databases such as PUBMED and Google Scholar. Queries were used to gather research articles, reviews, and studies up to the predetermined cut-off date. The collected data was then examined in order to find noteworthy patterns, methodologies, and outcomes pertaining to the investigation of MRS as a supplementary tool to morphologic and dynamic magnetic resonance imaging. The objective of this research is to enhance the detection accuracy of breast cancer, hence eliminating the need for unneeded benign biopsies.

Results: The detailed evaluation of MRS shows its ability to distinguish benign and malignant tumors, improving breast cancer diagnosis. This non-invasive method reveals tumor metabolism and physiological changes connected to cancer. This method may reduce unnecessary benign biopsies and improve breast cancer detection results. However, this technology needs further study to improve its methodology and sensitivity, making it a promising cancer research subject.

Conclusion: MRS is an auspicious non-invasive methodology that offers valuable insights into both the metabolic characteristics of tumors and the physiological changes associated with the malignant transformation in breast cancer. Extensive research has been conducted to explore the therapeutic uses of breast cancer imaging techniques, namely in the areas of diagnosis and evaluation of therapy efficacy. The relevance of MRS in clinical treatment has been shown in its ability to enhance the specificity of breast MRI, hence eliminating the need for biopsy of benign lesions. However, the selection of the most effective approach is still a topic of discussion. Additional research is required to enhance the methodology and sensitivity level.

Keywords: Proton Magnetic Resonance Spectroscopy; Breast Cancer; Pulse Sequence.



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Designing Comprehensive CT Image Quality Software for Quantitative Evaluation

Running title: CT Image Quality Software

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Abstract

Background: Computerized Tomography (CT) scanners require image quality testing before clinical use. To achieve this, tools like phantoms, as recommended by American Association of Physicists in Medicine (AAPM), are utilized. Image quality assessments, particularly quantitative methods, can be time-consuming and prone to inaccuracies. Therefore, having dedicated software is beneficial for enhancing accuracy and speed in evaluations.

This study aims to design software for CT image quality control phantoms. The software will include tests for uniformity and standard deviation, CT number accuracy, Modulation Transfer Functions (MTF) through three methods (Point Spread Function, Line Spread Function, and Edge Spread Function) using the pre-sampling method, Noise Power Spectrum (NPS), low-contrast resolution, and cupping artifact. Additionally, it will be capable of generating Mass/Electron density to CT number calibration curves (MDCT/EDCT) using 3D and 2D ROIs.

Materials and Methods: The software and Graphical User Interface (GUI) were developed using MATLAB. To validate the software, its results were compared with those from ImageJ, Excel, and manual calculations (the reference method).

Results: The calculation of MTF was influenced by the process of creating ROIs, which warrants further investigation in future studies. The initial evaluation procedures confirmed the software's results when compared to the reference methods. However, for clinical applications, additional testing with different scanners is required to ensure result repeatability.

Conclusion: This software offers eight quality tests for CT scanner images and the ability to generate the MDCT/EDCT curve used in radiotherapy treatment planning. It features a user-friendly GUI and the capability to perform complex and quantitative calculations of NPS, PSF, LSF, and ESF in seconds. Additionally, it can automatically determine the slit angle for LSF and ESF in the presampling method. Results can be easily exported to Excel by clicking a button for convenient storage.

Keywords: Computerized Tomography Imaging Quality Control; Dedicated Quality Assurance Software.



Efficacy of MR-Linac Guided Radiotherapy in Prostate Cancer Treatment MR-Linac in Prostate Cancer Therapy

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Abstract

Background: Prostate cancer is one of the most prevalent cancers affecting men worldwide, emphasizing the need for effective treatment modalities. Radiation therapy plays a crucial role in the management of prostate cancer, offering curative and palliative options. The integration of Magnetic Resonance Imaging (MRI) with a Linear Accelerator (Linac), known as MR-Linac, has emerged as a promising technology for improving treatment outcomes in prostate cancer.

This review examines the benefits, outcomes, and challenges of MR-Linac and MR-guided adaptive therapy for prostate cancer, while also discussing the significance of the disease and the limitations of conventional radiotherapy.

Materials and Methods: A comprehensive review was conducted to gather relevant information on radiotherapy treatment options for prostate cancer, with a specific focus on the application of MR-Linac technology. Databases such as PubMed, Scopus, and Google Scholar were searched using keywords including prostate cancer, MRI-guided radiotherapy, MR-Linac, and adaptive therapy. The collected data were carefully analyzed to provide a current perspective on the role of MR-Linac in the treatment of prostate cancer and its application in clinical practice.

Results: The introduction of MR-Linac technology has significantly transformed the landscape of prostate cancer treatment, offering a range of benefits while also presenting some challenges and limitations. MR-Linac provides superior soft tissue visualization, greatly improving the precision of target delineation during treatment planning. Clinical studies have established the safety and effectiveness of MRI-guided radiotherapy in achieving treatment outcomes comparable to conventional radiotherapy while minimizing late toxicities. MR-Linac technology enables real-time adaptation of treatment plans, ensuring precise radiation delivery to the target while minimizing exposure to healthy tissues, thereby enhancing patient safety. Functional imaging techniques, such as diffusion-weighted and dynamic contrast-enhanced imaging, play a crucial role in personalized treatment planning by incorporating tumor characteristics based on both anatomical and functional parameters. Challenges in MRI availability, costs, and dose calculations due to a lack of electron density data affect broader MR-Linac accessibility. Efforts to create synthetic CT images from MRI data, while promising, face ongoing challenges, especially for bony structures. Addressing challenges like imaging issues in low electron density regions, time-intensive adaptive planning, treatment of patients with implants or metallic devices, and the inability to deliver volumetric modulated arc therapy plans is crucial.

Conclusion: MR-Linac and MR-guided adaptive therapy have become valuable assets in prostate cancer treatment, offering personalized planning and real-time adjustments to enhance treatment results. Further research and clinical trials are required to confirm their long-term effectiveness and cost-effectiveness in managing prostate cancer.

Keywords: Magnetic Resonance Imaging with a Linear Accelerator; Prostate Cancer; Magnetic Resonance Imaging-Guided Radiotherapy; Adaptive Therapy; Magnetic Resonance Guided Radiotherapy.



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Validation of Brachytherapy Dosimetry Parameters with Geant4 Simulation

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Abstract

Background: In Image-guided Brachytherapy (IGBT) performed using Magnetic Resonance Imaging (MRI), sources must be simulated through dosimetry in the vicinity of the magnetic field before clinical tasks because the dose distribution may change due to the specific characteristics of each source. In this research, the complete structure of Ir¹⁹², Yb¹⁶⁹ and Co⁶⁰, common sources in clinical applications, were simulated and then dosimetric parameters were validated by Geant4. According to the American Association of Physicists in Medicine Task Group 43 (AAPM-TG43), for this purpose, it is enough to calculate only two factors of the dosimetry parameters of the simulated radioactive sources (the dose constant Λ , and the radial dose function $g(r)$). Because these sources are in the form of seeds or cores, the dose distribution is three-dimensional and cylindrical, so it can be considered symmetrical.

The purpose of validation is to ensure the accuracy of the simulation for brachytherapy sources and to evaluate the correct results in achieving accurate dose distribution.

Materials and Methods: In this research, we used the dose rate constant Λ and the radial dose function $g(r)$ for validation. First, the dose rate constant was obtained by calculating the dose and air kerma, and then the radial dose function was calculated by simulating and calculating the formula, the tables and graphs of each are attached. The geometry of the detector for all sources is a ring with an outer radius of 10.05 mm and an inner radius of 10 mm from the center (thickness of 0.05mm) and a width of 0.125 mm, so that up to a radius of 7 cm, the width value is 0.05 mm and in the radius of 8, 10, 12 and 15 cm it is equal to 0.15, 0.1, 0.75 and 0.2 mm, respectively. We considered the number of primary particles as 4×10^8 .

Results: We obtained the dose value at the reference point for three sources (Ir¹⁹², Yb¹⁶⁹ and Co⁶⁰) and replaced the amount of dose in the relationship of the radial dose function and compared the result with the value obtained in the reference paper, which is in good agreement with the error below two percent was obtained for each of the points. The results of the radial dose function obtained from the simulation of brachytherapy sources are presented in the form of tables and graphs obtained from the fitting of the 5th order function with a relative error of about 2%.

Conclusion: According to the values obtained for each source, air kerma, radial dose function and relative error calculation of less than 2%, it can be concluded that the simulation of the sources is accurate and correct, so the results of the analyzes are reliable.

Keywords: Association of Physicists in Medicine Task Group 43; Benchmarking; Dose Calculation; Geant4.



6th International TPCF Preclinical Imaging Symposium



Evaluation and Analysis of Magnetic Field Effect on Brachytherapy Sources

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Abstract

Background: Radiation therapy is one of the main methods of treating and controlling tumors. Patient's quality of life is directly related to the accuracy of treatment provided. Recently, with the advancement of radiation therapy methods in order to achieve this target and quality of treatment, radiation therapy systems based on image guidance have been created. This new technology is known as Resonance Imaging with a Linear Accelerator (MR-Linac) device. The reason for choosing the Magnetic Resonance Imaging (MRI) system compared to other imaging systems is the quality and superiority of the soft tissue image. Today, in some advanced cancer treatment centers in the world, brachytherapy is performed in the presence of a magnetic field using MRI imaging. There are three types of responses for electron behavior under the influence of magnetic fields according to Lorentz force. When the field is perpendicular to the direction of the electron's movement, its path deviates, when it is parallel, it moves in the same direction, and when it has an angle with the field lines, it moves in a spiral path towards the magnetic field lines Direction. According to this principle, the dose distribution in the perpendicular or parallel magnetic field can be narrower or wider.

The main purpose of this research is to investigate the effect of magnetic fields for the dose distribution of brachytherapy sources and the treatment planning algorithm under the guidance of MRI imaging.

Materials and Methods: In this research, simulation is done using the Monte Carlo code. The computational space called homogeneous phantom consists of a cube with dimensions 6×6×6 cm, which consists of 216.000 cells with dimensions of 1 mm and water content. Considering the effective distance in brachytherapy treatments and in order to facilitate the analysis of the large volume of data to draw the isodose curves, a cubic meshing was defined along all three coordinate axes, and the dose changes in the longitudinal interval ±3cm on the sides of the center of the source were calculated. The output was drawn in the form of isodose curves by MATLAB software through Geant4 meshing method and the difference between the curves in the state with and without the presence of magnetic field was expressed by the Gamma Index parameter and with the criteria of 3% and 3 mm.

Results: The error value for the dose obtained in the farthest cell from the center of the source as the maximum error was less than 5%, in other words, in the whole simulation, the error was below 5%.

Conclusion: The effects of magnetic field on the dose distribution caused by iridium-192 and ytterbium-169 were observed to be ineffective, as a result, it is possible to ensure the safety of brachytherapy treatment with these sources in the presence of magnetic fields. However, regarding Cobalt-60 due to the dispersion of isodose curves in different field intensities, necessary considerations are recommended.

Keywords: Brachytherapy, High Dose Rate Sources, Magnetic Field, Monte Carlo.



The Role of the Generative Adversarial Network in Medical Image Reconstruction: A Systematic Review

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Abstract

Background: In the realm of medical imaging, obtaining clear, high-resolution images is challenging due to a multitude of factors encompassing the intricacies of imaging systems, diverse imaging environments, and the potential impact of human-related variables. The imperative initial step in the assessment of medical images involves medical image processing, a field that leverages the power of machine learning and deep learning models to cultivate intelligent systems, thereby imbuing these images with heightened interpretability and enhancing diagnostic efficiency. The advent of Generative Adversarial Networks (GANs) represents a transformative technological breakthrough, ushering in a new era in the realm of medical image analysis. GANs have introduced a robust framework for the manifold applications of medical images. These applications vary from the enhancement of medical images to their precise segmentation, accurate classification, meticulous reconstruction, and even synthesis.

This study aimed to give a general insight into the role of Generative Adversarial Networks (GANs) in medical image reconstruction. This comprehensive background provides the necessary context for understanding the pivotal role of GANs in revolutionizing the domain of medical imaging and underscores their impact on the development of sophisticated and intuitive systems for the advancement of medical diagnostics.

Materials and Methods: PubMed, ScienceDirect, Web of Science databases, and Google Scholar were explored using different combinations of keywords: “Generative Adversarial Networks (GANs)”, “Deep Learning”, “Image Reconstruction”, “Medical Imaging” and “Artificial Intelligence”. Also, an additional search was performed on Semantic Scholar. Finally, 20 most related and recent papers were included in the study.

Results: Generative Adversarial Networks (GANs), consisting of a generator and a discriminator neural network in a competitive framework, have demonstrated their effectiveness in medical image reconstruction. They excel in generating high-fidelity images from incomplete medical data by training on complete image datasets and leveraging this knowledge to fill in the gaps. GANs also play a pivotal role in generating multimodal datasets from a single modality source, thereby expanding the diversity of training data for improved accuracy in medical image analysis. This versatility of GANs finds practical application in various algorithms designed for medical image reconstruction, such as Medical Image Reconstruction using Generative Adversarial Networks (MirGAN) and GAN-Based Medical Image Super-Resolution via High-Resolution Representation Learning (Med-SRNet). These techniques are tailored to tasks like medical image reconstruction and super-resolution, enhancing the quality of medical images. As a result, they simplify the process of image analysis and diagnosis in the field of medicine. In this context, GANs have emerged as a transformative technology, significantly contributing to the improvement of medical imaging quality and the facilitation of more accurate analysis and diagnosis of medical conditions.

Conclusion: In summary, although GANs have exhibited substantial promise in the realm of medical image reconstruction, they have also their challenges. These limitations encompass restricted data accessibility, intricate computational demands, interpretability issues, susceptibility to overfitting, and quality control concerns.

Keywords: Generative Adversarial Networks; Deep Learning; Image Reconstruction; Medical Imaging; Artificial Intelligence.

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Theranostic Agents for Image-Guided Boron Neutron Capture Therapy

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Abstract

Background: Boron Neutron Capture Therapy (BNCT) is a kind of targeted radiotherapy that appears to be a promising tool in cancer treatment, by selectively concentrating boron compounds in tumor cells. Essentially, boron-10(^{10}B) atoms capture the thermal neutrons and instantly decay to produce an alpha particle (^4He), a lithium nucleus (^7Li), and low Linear Energy Transfer (LET). Hence, these particles provide high energy over a short pathway to damage cancer cells, which have significantly more boron-compound uptake than normal cells. BNCT has been used to treat glioblastoma, head and neck cancer, hepatocellular carcinoma, salivary gland carcinomas, etc. In addition, a large number of boron-containing compounds have been evaluated within three generations, consisting of 1) Boric acid and its derivatives 2) sodium borocaptate (BSH), and the boron-containing amino acids such as ^{10}B -*p*-boronophenylalanine (BPA) 3) boronated amino acids, peptides, MABs, liposomes, boron-containing nanoparticles.

An important factor often considered a drawback of BNCT is the heterogeneous distribution of boron within the tumor, leading to ambiguity in the calculated dose distribution. This challenge can be overcome using theranostic agents, which combine imaging and therapy, causing precision therapy. This study aims to review the well-published imaging probes that serve as boron-10 delivery agents but also for the estimation of boronated compound's biodistribution.

Materials and Methods: A literature search was carried out in four electronic scientific databases (e.g. PubMed, ScienceDirect, Google Scholar, and Web of Science). Appropriate data from 1988 to 2023 was collected and compiled in this study.

Results: BSH and BPA are two boron-containing compounds used for clinical applications and they have paved the way for the design of different theranostic agents. In 1991, ^{18}F -labeled 2-borono-4-fluoro-L-phenylalanine (^{18}F -FBPA) was presented by Ishiwata et al. for monitoring the biodistribution of BPA prior to BNCT, using Positron Emission Tomography (PET). Early clinical findings with [^{18}F] FBPA confirmed the potential of PET to screen different tumor lesion candidates of BNCT. Except for ^{18}F , the other radioisotopes may be combined with boron compounds, allowing monitoring and quantification in preclinical studies. Gold nanoparticles labeled with iodine-123 or 124, incorporation of gallium-68(^{68}Ga) and copper-64(^{64}Cu) into the nanoparticle structures, and BSH-peptide labeled with ^{64}Cu are examples of PET imaging probes utilized in animal investigations to detect boron-containing compounds. Magnetic Resonance Imaging (MRI) has been also used for monitoring the tumor mass before and after BNCT. Several in vivo studies have reported various compounds containing both ^{10}B and Gadolinium (Gd) or iron (Fe) as a new generation of theranostic agents for BNCT.

Conclusion: Up to now, the development of new ideal boronated compounds, which have tumor-normal tissue and tumor-blood ratios of more than 3 with low toxicity and constant concentration during BNCT, is an important issue. On the other hand, theranostic agents for image-guided BNCT should behave similarly to their therapeutic agents. Nowadays, [^{18}F] FBPA is an appropriate compound for this purpose and can be used clinically to assess the distribution of BPA in patients by many investigators. Future horizons of theranostic agents will be more selective and specific compounds through designing novel boron-contacting agents.

Keywords: Boron Compounds; Boron Neutron Capture Therapy; Cancer Treatment; Cancer; Theranostics.



Improving Detection of Breast Cancer with Unet++ Deep Learning Framework in Digital Mammography

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Abstract

Background: Breast cancer is the most prevalent cancer among women, resulting in millions of fatalities each year. Accurate segmentation of breast masses is critical for early detection of breast cancer, potentially leading to enhanced diagnosis and reduced mortality rates. Mammography is a common screening tool for detecting breast cancer.

Segmentation of mammograms manually is a time-consuming and subjective task. Hence, it is critical to develop an automated method that can overcome challenges such as low signal-to-noise ratio, high false positive rates, and various mass shapes and sizes. In this paper, we present an automated approach for mass segmentation, which employs a comprehensive pre-processing pipeline to effectively address these challenges.

Materials and Methods: The proposed method consists of two phases; the initial phase consists of pre-processing, comprising artifact removal, denoising, contrast enhancement, image cropping, resizing, and mammogram augmentation. The subsequent phase involves model design, where UNet++ is utilized as an encoder-decoder-based network to segment breast masses. The encoder efficiently captures significant information from various regions in the input image, while the decoder reconstructs the spatial location of the target region. To evaluate the performance of the proposed method, we conducted experiments on the publicly accessible CBIS-DDSM dataset.

Results: Our findings demonstrate the promising results with an accuracy of 96.4%. The precision rate of 84.2% and sensitivity rate of 81.3% further support the method's proficiency in segmenting breast masses. The Dice Score Coefficient measuring at 77.1% and the Jaccard index at 65.1% also confirm its reliability in identifying the target region.

Conclusion: Employing UNet++ with a pre-processing pipeline in digital mammography has demonstrated favorable outcomes concerning precise segmentation of breast masses. The promising results of this approach indicate its potential to significantly enhance early detection of breast cancer.

Keywords: Breast Cancer; Mammography; Deep Learning; Semantic Segmentation; UNet++.



6th International TPCF Preclinical Imaging Symposium



The Applications of Machine Learning in The Preclinical Laboratory Researches

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Abstract

Background: Machine learning is a branch of Artificial Intelligence that can learn and adapt without following explicit instructions. In the last decade, machine learning allows the analysis of complex and large data sets and has the potential to improve healthcare.

The aim of this review article was to identify the importance of ML in the preclinical lab. Throughout this period, a significant volume of information is amassed, posing a challenge for even a team of experienced specialists to effectively process and analyze. Given the magnitude of the data, achieving a satisfactory level of accuracy in the neural network data model becomes feasible.

Materials and Methods: In this review article, the data was collected from international scientific databases, including Google Scholar, Scopus, PubMed, and Elsevier. The key words “Machine Learning”, “Artificial Intelligence” and “preclinical Researches” were searched.

Results: The article explores the approach to conducting preclinical laboratory research, focusing on the methodology employed. The method involved conducting a Preclinical Validation Study, utilizing the Ocular Disease Intelligent Recognition (ODIR) database, which consists of around 4,000 color fundus images along with diagnostic results from specialists. The accuracy of the constructed model was obtained together with the optimal hyperparameters.

Conclusion: It is suggested to use ML systems for the diversity of research activities that needs to analyze large data sets.

Keywords: Machine Learning; Hyperparameters; Preclinical Researches, Convolutional Neural Network.



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Radiogenomics in The Analysis of Medical Images and Prospects for its Use in Personalized Treatment

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Abstract

Background: Radiation therapy, a highly effective cancer treatment modality, is widely used for eliminating cancer cells. However, it is associated with side effects that can significantly impact the patient's quality of life. Understanding these effects solely based on dosimetric, therapeutic, clinical, and demographic factors is not sufficient. Genetic factors have been found to play a role in radiation-induced adverse effects, highlighting the importance of exploring these factors for personalized cancer treatment. Radiogenomics is an emerging field that focuses on studying the genomic changes underlying the response of normal and tumor tissues to radiation. Its goal is to establish a connection between imaging features (radiomic phenotypes) and genetic factors such as gene expression patterns and mutations for disease treatment and prevention. This interdisciplinary approach involves using advanced imaging modalities like Magnetic Resonance Imaging (MRI), Computerized Tomography (CT), and Positron Emission Tomography (PET) to investigate the relationship between imaging features and genomic data in various cancers. The objective of this research is to provide a comprehensive review of recent advances in radiogenomics.

Materials and Methods: The research methodology includes a thorough analysis of relevant literature to gather information on the advancements in radiogenomics. Keywords related to radiogenomics and personalized medicine are used to identify relevant sources, and databases like PubMed and Web of Science are searched for reputable studies. The analysis focuses on the connection between imaging features and genomic data, as well as the potential applications of radiogenomics in precision medicine.

Results: Radiogenomics plays a crucial role in improving the customization of radiation therapy treatments, reducing side effects, and establishing correlations between genotypes and imaging phenotypes for treatment decision-making. Furthermore, it aids in determining the most informative and relevant image types for each disease group, thereby enhancing effectiveness in diagnosis and treatment. Radiogenomics serves as a non-invasive and cost-effective tool for comprehending the molecular basis of tumors and developing imaging biomarkers as alternatives to genetic testing. The analysis of gene expression patterns before and after radiation therapy helps identify patterns associated with an effective response to radiotherapy, including genetic resistance patterns. Recent advancements in artificial intelligence have contributed to the field of radiogenomics by enhancing predictive modeling capabilities through the extraction of phenotypic data from images, coupled with genomic and clinical information. Despite limitations such as reproducibility challenges, tumor heterogeneity, complex gene-pathway correlations, poor reproducibility of radiomic features, and the need for improved computational tools, radiogenomics holds significant potential in precision medicine. Numerous studies underscore the potential applications of radiogenomics in precision medicine, encompassing breast cancer, pelvic cancer, and prostate cancer. It highlights the role of radiogenomics in addressing challenges associated with traditional genetic tests through innovative imaging approaches.

Conclusion: In conclusion, the utilization of personalized therapeutic strategies incorporating radiogenomics has the potential to significantly enhance treatment outcomes and revolutionize cancer care, ultimately leading to an improvement in the quality of life for patients.

Keywords: Radiogenomics; Imaging Genomics; Radiation Genomics; Personalized Medicine; Precision Medicine.

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Deep Vision Transformer Model for the Prediction of Antidepressants Outcome in Major Depressive Disorder Using Raw EEG Signals

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Abstract

Background: Major Depressive Disorder (MDD) is a high prevalence disease worldwide and needs accurate and timely treatment. However, antidepressants as the first line treatment for the MDD patients are mostly selected based on the trial and error. Therefore, the prediction of response to a specific antidepressant is necessary to prevent ineffective treatment sessions and improve the quality of life for MDD patients. The recent advance in the deep learning architectures which is called Transformer model is based on the attention mechanism and showed superior performance in multiple tasks including signal and image classification.

In the present research we aim to develop a new deep learning model based on Vision Transformer (ViT) architecture to classify the Responders (R) and Non-Responders (NR) to the antidepressants using the pre-treatment Electroencephalography (EEG) signals.

Materials and Methods: Thirty subjects diagnosed as MDD patients based on DSM-IV manual criteria included in this study. The depression severity was calculated based on Beck Depression Inventory (BDI) and the Selective Serotonin Reuptake Inhibitors (SSRIs) prescribed as antidepressants for all patients. 19-channel EEG signal acquired before the treatment initiation in the resting-state with the eyes-closed situation for 5 minutes by 256 Hz sampling rate. The response to the treatment is defined as 50% decrease in the BDI score after the treatment completion. The EEG signal was pre-processed using EEGLAB toolbox in MATLAB to remove the noises from the recorded signal. Firstly, the EEG signal was band-pass filtered between 1 Hz and 40 Hz and then the Artifact Subspace Reconstruction (ASR) package from EEGLAB was used to detect and remove the highly contaminated parts of the signal. Finally, Independent Component Analysis (ICA) method was used to find the signal components that were not originated from the brain and remove them. Three-dimensional images were constructed by concatenating the consecutive 0.5 second segments of the raw EEG signals with 70 percent overlap between segments to be fed into the deep learning model. The ViT model constructed by 6 encoder layers where each encoder includes a multi-head attention model with 6 heads. The model was trained and validated by using 80 percent of the input data to achieve highest accuracy and finally tested on 20 percent unseen test data.

Results: After 50 epochs of the training and validation of the proposed model, learning curves including accuracy and loss curves showed that the model was converged. The training accuracy of 96% and validation accuracy of 92% achieved. The test results using the unseen test data gained an accuracy of 91% which represents the generalizability of the model. The proposed model achieved a superior performance in the prediction of R and NR in MDD treatment using raw EEG signals. Therefore, such a model can be utilized in clinical facility to prevent patients from starting an ineffective treatment. This study should be replicated using large sample sizes and cross-validation methods.

Conclusion: The deep learning model developed in this study based on transformer models achieved 91% test accuracy in the prediction of Responders and Non-Responders to the antidepressants using raw EEG signals.

Keywords: Major Depressive Disorder; Electroencephalography; Vision Transformer; Response Prediction.



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Role of Cytokines Therapy in Cancer Treatment

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Abstract

Background: The number of cases reported with cancer diagnosis has been enhanced through the last 3 decades and the demand of seeking for beneficial treatment has been more significant. Recently, cytokines therapy for cancer has demonstrated new methods which some of them were considered beneficial. Cytokines serve as pivotal regulators of innate and adaptive immunity, facilitating intercellular communication among immune cells in close proximity and also have the ability to impede the advancement and progression of cancer. Conversely, cancer cells can react to cytokines originating from the host, which promote cellular growth, suppress apoptosis, and facilitate the invasion and spread of cancer to other parts of the body.

The aim of this review article is to provide information about preclinical researches of cytokine-based cancer treatments which is able to manifest the advantages and disadvantages of cytokines through cancer therapy that some of them in the future requires to be fixed or improved under investigational preclinical trials.

Materials and Methods: In this review article, the data was collected from international scientific databases, including Scopus, Google Scholar, PubMed, and Elsevier. The key words cytokine, cancer treatments and preclinical Researches were searched.

Results: In this article clinical trials including evaluating and investigating the efficacy about role of INF- γ as an adjuvant treatment of completely resected high-risk melanoma patients or several refractory malignancies and High-dose interleukin-2 (HDIL-2) for treatment of metastatic renal cell cancer and melanoma were discussed. the initial promise shown in preclinical experiments, the use of cytokines as a monotherapy has not delivered the expected efficacy. One of the main challenges is the severe dose-limiting toxicities associated with cytokine therapy. nevertheless, with proper dosing strategies and improved understanding, these toxicities can be managed. It is now recognized that cytokines can induce the production of immune-suppressive factors, suppressive cells, and cellular checkpoints, without consistently eliciting a specific response against the tumor. This highlights the need for combination therapies and a more comprehensive approach to harness the potential of cytokines in cancer treatment.

Conclusion: In some types of cancers cytokine therapy was beneficial thus It is suggested to apply the approved cytokine therapies for treating cancers even as an adjuvant component.

Keywords: Cytokine; Cancer Treatments; Preclinical Researches.



Surface Functionalized Laser Ablated Mineral Paper: A Feasible Scaffold for Enhanced Bone Regeneration

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Abstract

Background: Despite remarkable progress in bone regenerative medicine, developing a cost effective approach for osteocyte regeneration on matrixes with proper three-Dimensional (3D) morphological form and mechanical strength is still challenging. Finding a proper scaffold having optimized parameters such as chemical composition, mechanical properties and surface characteristics can improve bone repairing and regeneration for clinical applications. Stone paper (also known as mineral paper) is a new type of papers that consists of calcium carbonate and High-density Polyethylene (HDPE) that has great potential to be introduced as a cost-effective composite for bone tissue engineering applications.

Here, we aimed to develop a feasible platform to improve artificial bone generation that is capable of mimicking bone tissue microenvironment. In this regard, patterned stone paper with laser ablation was evaluated for bone tissue engineering purposes. Moreover, to improve hydrophilicity and consequent cell regeneration, polydopamine coating was examined on patterned surfaces.

Materials and Methods: Two different designs were selected to be ablated using CO₂ Laser for using as 3D matrix for bone regeneration. The ablated papers were then immersed in a solution in order to be coated with polydopamine. Physicochemical characterization of obtained scaffolds was performed using XRD, SEM, ATR and WCA to verify both effects of laser ablation and surface modification. Also, MTT test was done to determine the level of cytotoxicity.

Results: XRD test proved that the laser process didn't have any destructive effect on the crystal structure of calcium carbonate in mineral paper scaffold. We have optimized patterns of laser ablation based on data obtained by the SEM less distortions and cracks. Although the water contact angle of the paper has been increased about 30 degrees after laser ablation process, coating the paper with polydopamine has positive effects on surface roughness, wettability, porosity, mechanical properties, and specific surface area. Structural characterization of the scaffolds by ATR demonstrated that polydopamine coating had significant effect on physicochemical properties of matrix mainly in interconnected pores without any toxicity confirmed by MTT assay.

Conclusion: Based on obtained results, it can be concluded that the surface modified laser ablated rich mineral paper scaffold has great potential for promoting cell proliferation and osteogenic differentiation. Combination physical and chemical modification by Co₂ laser ablation and polydopamine coating have led to improved scaffold properties for future clinical applications.

Keywords: Scaffold; Tissue Engineering; Rich Mineral Paper; Polydopamine; Laser Ablation.



6th International TPCF Preclinical Imaging Symposium



A Mixture of Compressed Sensing and Half-Scan Methods for Accelerating MRI Image Reconstruction from Under-Sampled k-Space Data

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Abstract

Background: Magnetic Resonance Imaging, MRI, although as one of the most advanced medical imaging equipment is well known but compared to other medical imaging systems needs more time to imaging, so it has caused the patient dissatisfaction.

Materials and Methods: According to the recently researches, filling the image data in a space of information that called 'k-space', in the process of image reconstruction, is the main reason of slow MRI. Image reconstruction methods for accelerating like half scan based on image reconstruction by using only a part of k-space is used in MRI systems today, but this method is associated with lower SNR image. Recent research on the theory of compressed sensing has been opened a new approach in the MRI image reconstruction. Based on this theory can be recover the signal with sampling rate less than is expressed in Nyquist theorem.

Results: In this study, after introducing procedures to accelerate the MRI image reconstruction, with an emphasis on compressed sensing and half-scan methods as the two important methods based on image reconstruction with undersampled k-space, the proposed method is expressed. This method is a combination of half scan and compressive sensing method.

Conclusion: Simulation shows that to add compressed sensing to half-scan method, while maintaining acceleration of image reconstruction with 62.5%, could be increased SNR as much as 0.42 dB and reduce the relative error of the image as much as % 0.13 compared to use compressive sensing alone.

Keywords: Magnetic Resonance Imaging; Compressing Sensing; Half Scan; K-Space; Under-Sampling.



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Iterative Image Reconstruction of Optical Computed Tomography for Gel Dosimetry Evaluation of Iterative Algorithms for an in-house System

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Abstract

Background: Dose distribution measurement in radiotherapy became very important especially in accurate dose delivery systems. Gel dosimeters have the ability to accurately measure the complex 3D dose distributions which other conventional dosimeters cannot handle. Optical Computed Tomography (OCT) was proposed to provide a simple, cheap and clinically accessible device for accurate and 3D dose readout. Among multiple setups proposed for OCT imaging, Cone-Beam OCT based on visible light source and Charge Coupled Device (CCD) camera provides faster dose readout and relatively cheaper setup. 3D image reconstruction of the Cone-Beam OCT for the gel dosimeters is a crucial task which directly impacts on the image quality and dose measurement. The FDK method is the primary algorithm for Cone-Beam OCT image reconstruction but is highly sensitive to the number of acquired projections and provide poor resolution. Hence, the iterative image reconstruction methods was proposed which utilize optimization algorithms to minimize the specific cost functions in multiple iterations.

The main objective of this work was to compare and validate multiple iterative image reconstruction algorithms for OCT gel dosimetry device developed in our lab.

Materials and Methods: An in-house OCT system was developed that utilizes cone beam configuration. A MAGIC-f gel was produced for the dose readout. The light source was configured as a 5*5 array of red LEDs by 650nm wave length. A light diffuser with 10cm*10cm dimension attached to the light source to make a unified light intensity. Gel is located in a vial with 1 cm diameter that itself located in a 25cm*25cm water tank including a matching liquid. The CCD camera obtains images in 12 bit resolution. For obtaining projections from multiple views, the gel vial is attached to a stepper motor shaft that can rotate 1.8 degree in each step to acquire 200 projections for reconstructing a 3D tomographic image. Three powerful iterative image reconstruction methods named Maximum Likelihood Expectation Maximization (MLEM), Simultaneous Algebraic Reconstruction Technique (SART) and Separable Quadratic Surrogates (SQS) were utilized along with FDK to evaluate the dose readout accuracy of our in-house OCT system.

Results: All iterative methods were continued for 50 iterations and their results converged to the optimal solution. The Full Width Half Maximum (FWHM) was calculated for each of these methods as a measure of spatial resolution. The FWHM of all methods are calculated and the FDK, MLEM, SART and SQS gained 6.3mm, 3.2mm, 3.5mm, 3.9mm for FWHM respectively. Comparison of reconstruction profiles shows that iterative methods suppress the noise in the reconstructed image and gain a higher signal to noise ratio. Therefore, the iterative methods can successfully be used for image reconstruction of our OCT system.

Conclusion: Iterative image reconstruction techniques can improve image quality and the developed OCT system performs well on dose readout and can be a promising tool for calibration of radiation based systems.

Keywords: Gel Dosimetry; Optical Computed Tomography; Iterative Image Reconstruction.



The Predictive Value of Targeted Ultrasound in the Diagnosis of Pediatric Renal Scarring

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Abstract

Background: Vesicoureteral reflux is an important risk factor of recurrent pyelonephritis and subsequent renal scanning. Today, Dimercaptosuccinic Acid (DMSA) scan is the chosen method of diagnosis and follow-up of renal scar treatment. This study was conducted to determine the diagnostic value of ultrasound in comparison with nuclear scanning for the diagnosis of renal scars in children.

Materials and Methods: The present study was a cross-sectional study. In this study, 150 children who referred to the Doctor Sheikh Hospital between 2019-2020 due to urinary tract infection were examined after obtaining written informed consent. Demographic and clinical data of patients were collected and recorded in a checklist. Six months after the treatment, the patients were examined for the presence of renal scar by ultrasound done by a pediatric radiologist. The results of the DMSA scan were evaluated by a nuclear medicine specialist without knowing the results of the ultrasound. Then the results were recorded subjectively in the respective checklists. All the obtained data were analyzed by software SPSS version 23 and specificity, sensitivity and positive and negative predictive values of the ultrasound compared to nuclear scan were determined.

Results: In this study, 136 children with an average age of 5.10 ± 3.29 years, in which 55 of them (40.4%) were boys, were examined. In total, 98 patients (72.1%) had a history of urinary tract infection, four patients (2.9%) had a history of renal anomalies in postnatal ultrasound, and 83 patients (61.0%) had renal reflux in VCUG. According to the diagnostic criteria, 55 patients (40.4%) had renal scarring in the nuclear scan and 42 patients (30.9%) in the ultrasound, and there was a significant agreement between the results of the ultrasound and nuclear scanning in the diagnosis of renal scarring in children ($P < 0.001$, $K = 0.699$). The frequency of history of reflux and history of urinary infection was significantly higher in patients with renal scar diagnosed by ultrasound ($P < 0.05$). The sensitivity and specificity of ultrasound for the diagnosis of renal scar were 70.9% and 96.3%, respectively. Among the ultrasound findings, the highest sensitivity was related to the reduction of the thickness of the cortex (69.1%) and the highest specificity was related to the increase of the echo cortex, the fading of the border of the pyramid and the abnormal contour of the kidney was 100%.

Conclusion: Targeted ultrasound with a sensitivity of 70.9% and a specificity of 96.3%, as a quick, inexpensive, and available method, can be used to diagnose renal scarring in children with a high and favorable diagnostic power.

Keywords: Ultrasound, Renal Scar, Children.



Evaluation of the Distribution of Radionuclide Production during Proton Therapy for Monitoring the Proton Range for Different Incident Proton Energies

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Abstract

Background: Proton therapy has shown promise in treating different type of cancer which cause fewer side effects than traditional radiation. Nuclear fragmentation reactions produce different radionuclides such as C^{10} , C^{11} , N^{13} , and O^{15} during proton therapy. Reliable radioisotopes production information is a prerequisite for monitoring the proton range in vivo proton treatment.

In this context, the distribution of radionuclide production during proton therapy for different incident proton energies was analyzed to provide a correlation between the radionuclide yields with the proton dose distribution for monitoring the proton range.

Materials and Methods: In the GATE Monte Carlo code, a homogeneous cylindrical PMMA phantom was irradiated with mono-energetic proton beams at three distinct energies: 90,120,150 MeV. Then we investigated the spatial distribution of produced radioisotopes C^{10} , C^{11} , N^{13} , and O^{15} along with the proton dose distribution.

Results: For all incident proton energies, results show that using the distribution of O^{15} and C^{11} radioisotope production, the proton range can be estimated with an accuracy of about 7 mm and 10 mm, respectively. For proton energies of 90, 120, and 150 MeV, the proton range was determined at the position of 54.5, 90.5, and 134.5 mm from the entrance of the PMMA phantom. The position of 80% fall-off in efficiency of distribution of carbon 11 radioisotope for proton energies 90, 120, and 150 MeV were determined 44.5, 80.5, and 123.5 mm, respectively, which provides the accuracy of 10, 10, and 11 mm, respectively, for estimating the proton beam range. The position of 80% fall-off in efficiency of distribution of Oxygen 15 for proton energies of 90, 120, and 150 MeV were determined 47.5, 84.5, and 127.5 mm, respectively, which provides the accuracy of 7, 6, and 7 mm, respectively, for estimating the proton beam range. The position of 80% fall-off in efficiency of the total four isotopes (Carbon-10, Carbon-11, Oxygen-15, and Nitrogen-15) for proton energies of 90, 120, 150 MeV were determined as 44.5, 84.5 and 124.5 mm, respectively, which provided a constant accuracy of about 10 mm for all of isotopes.

Conclusion: Since C^{10} and N^{13} radioisotopes have low production efficiency, range estimation via these radionuclides is somewhat impossible. Calculation of Δ fall-off correlation quantity for the four radioisotopes O^{15} , C^{11} , C^{10} , and N^{13} show that for all three incident proton energies, allowing to calculate the range of protons with an accuracy of about 10 mm. In this research, the spatial distribution of radioisotopes produced during proton therapy can be used to estimate the range of proton.

Keywords: Proton Therapy; Proton Range; Radioisotope.



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Report of a Case of Tonsillar Squamous Cell Carcinoma in a 13-Year-Old Male Lhasa Apso Dog in Iran

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Abstract

Background: The field of comparative oncology has garnered significant interest within the scientific community. Exploring tumors in animals can pave the way for studying tumors in humans, and vice versa. While primary tonsillar carcinoma in dogs is infrequently reported in comparison to non-tonsillar oral carcinomas, it exhibits a higher likelihood of local metastatic disease (up to 73%).

Materials and Methods: Squamous Cell Carcinoma (SCC) predominantly affects the digital region, oral cavity, and skin. Although the exact cause of this tumor remains unknown, there was an initial suggestion that dogs residing in urban areas are more susceptible to tonsil neoplasia. A 13-year-old intact male Lhasa Apso dog was referred to the clinic due to the presence of an abnormal mass on the left tonsil within the oral cavity.

Results: The dog exhibited normal appetite, food and water consumption, breathing rate, heart rate, Capillary Refill Time (CRT), body temperature, and blood test results. Radiographic imaging of the dog's head and a biopsy of the abnormal mass in the left tonsil were performed. Histopathological examination and immunohistochemical tests confirmed the diagnosis of basaloid squamous cell carcinoma. Treatment options encompass surgery, Radiotherapy (RT), chemotherapy, or a combination thereof. The owner of the dog opted not to pursue chemotherapy as a treatment option for the animal. Dogs diagnosed with tonsillar cancer typically have a short overall survival, and the prognosis ranges from poor to guarded.

Conclusion: Eventually, after one year, when the tumor had significantly increased in size, the dog in question was euthanized with the owner's consent.

Keywords: Tonsil, Dog, Cancer, Squamous Cell Carcinoma; Chemotherapy.



6th International TPCF Preclinical Imaging Symposium



A Review Article on Diagnostic Imaging Applications in the Diagnosis of Infectious Diseases in Small Animals

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Abstract

Background: This study takes a comprehensive approach to examine the different diagnostic imaging methods used for diagnosing infectious diseases in small livestock. To provide a thorough analysis of the topic, we have conducted an extensive literature review, analyzed case studies, and sought expert opinions. Diagnostic imaging techniques, including radiology, ultrasound, and Magnetic Resonance Imaging (MRI), play a vital role in accurately and promptly diagnosing infectious diseases in small livestock animals. These imaging methods enable the identification and localization of infectious agents, evaluation of organ involvement, and assessment of disease progression. Infectious diseases rank as the second leading cause of death globally. Noninvasive small-animal imaging has emerged as a crucial research tool for studying infectious diseases in preclinical settings.

Materials and Methods: Small animal imaging has greatly advanced our comprehension of disease progression and clinical investigations related to drug development. Through noninvasive imaging research, we can gather more comprehensive information by conducting longitudinal studies on animal models that mimic human diseases. In recent decades, various imaging methods for small animals have been utilized in the research of infectious diseases. These include MRI, Computed Tomography (CT), Positron Emission Tomography (PET), Bioluminescence Imaging (BLI), and intravital imaging. The aim of this study is to explore the effectiveness of diagnostic imaging techniques like radiology, ultrasound, MRI, and CT scan in diagnosing infectious diseases in small livestock, specifically bacterial, viral, parasitic, and fungal infections. Radiology plays a crucial role in identifying bone lesions, lung diseases, and gastrointestinal abnormalities. Ultrasound allows for the clear visualization of soft tissue structures, identification of abdominal masses, and assessment of fluid buildup. MRI offers comprehensive anatomical and pathological data, aiding in the diagnosis of brain infections, spinal infections, and musculoskeletal infections.

Results: This study emphasizes the important role of diagnostic imaging techniques in diagnosing infectious diseases in small livestock. By providing a thorough summary of the uses of radiology, ultrasound, MRI, and multiple-modality imaging, this research contributes to the existing knowledge about the application of these methods in veterinary medicine. The findings of this study contribute to a better understanding of the advantages of diagnostic imaging in helping with quick and accurate diagnoses. This leads to improved disease management and animal welfare. Given the growing occurrence and impact of infectious diseases in small livestock, the insights from this research can assist veterinarians, researchers, and animal health professionals in making well-informed decisions about using various diagnostic imaging techniques.

Conclusion: Additionally, this study highlights the potential for further advancements and innovation in veterinary diagnostic imaging. It urges investment and research in this field to enhance the quality of care for small livestock animals.

Keywords: Imaging Studies; Small Animals; Infectious Diseases; Magnetic Resonance Imaging.



Assessing Sensitivity and Scatter Fraction in a PET Scanner with Physical Collimation: A Monte Carlo Study

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Abstract

Background: Positron Emission Tomography (PET) is a vital diagnostic imaging modality in nuclear medicine. PET relies on the detection of 511 keV gamma rays resulting from the annihilation of positron-emitting radionuclides. However, PET images are susceptible to various events, including true coincidences, scatter coincidences, and random coincidences. Scatter coincidences can distort image quality and accuracy.

As mentioned earlier there are three main events true, scatter, and randoms. Scatter coincidences can lead to the misplacement of radionuclides within the body, and as scatters enter the detector obliquely, a physical collimator may have the potential to reduce them. This research aims to assess the sensitivity and scatter fraction of a PET scanner in the presence of a physical collimator.

Materials and Methods: In the GATE Monte Carlo code, a homogeneous cylindrical Polymethyl Methacrylate (PMMA) phantom was irradiated with mono-energetic proton beams at three distinct energies: 90,120,150 MeV. Then we investigated the spatial distribution of produced radioisotopes C^{10} , C^{11} , N^{13} , and O^{15} along with the proton dose distribution.

Results: To accomplish this objective, the Siemens Biograph Vision PET scanner with 38 detector modules was used. Each module consisted of 4 (trans axial) \times 2 (axial) mini-modules of a 5 \times 5 LSO detector array. Each individual LSO crystal, measuring 3.2 mm \times 3.2 mm \times 20 mm, was simulated and validated using the GATE Monte Carlo simulation toolkit. Subsequently, three commercial Siemens collimators, namely low-energy high-resolution, low-energy all-purpose, and low-energy all-purpose with a squared shape hole, were applied to the PET scanner. Sensitivity and scatter fraction were evaluated based on National Electrical Manufacturers Association (NEMA) NU2-2018 standards.

Conclusion: Physical collimators, when strategically applied, offer a potential solution to improve PET imaging by reducing scatter events while maintaining reasonable sensitivity, enhancing the overall effectiveness of this vital diagnostic modality. The results with the LEAPS collimator are promising, suggesting that with an optimal collimator design, it is possible to reduce scatter rays with a minimal reduction in sensitivity.

Keywords: Positron Emission Tomography; GATE; National Electrical Manufacturers Association; Monte Carlo Simulation.



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Radio Protective Effect of Black Mulberry Extract on Radiation Induced Damage in Bone Marrow Cells and Liver in the Rat

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Abstract

Background: Ionizing radiation by producing free radicals induces tissue oxidative stress and has clastogenic and cytotoxic effects.

The radioprotective effect of Black Mulberry Extract (BME) has been investigated on liver tissue and bone marrow cells in the rat.

Materials and Methods: 200 mg/kg BME injected intraperitoneally to the forty-eight male wistar rats three days before and three days after 3 Gy and 6 Gy gamma irradiation, The frequency of micronucleated polychromatic erythrocytes (MnPCEs), micronucleated normochromatic erythrocyte (MnNCEs) and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte +normochromatic erythrocyte) were calculated. In addition, the level of Malondialdehyde (MDA) and Superoxide Dismutase (SOD), total thiol content and catalase activity was determined in rat's liver.

Results: BME significantly reduced the frequencies of MnPCEs and MnNCEs and increased PCE/PCE + NCE ratio in rat bone marrow compared to the non-treated irradiated groups. Moreover, this concentration of BME extract decreased the level of MDA and SOD, as well as enhanced the total thiol content and catalase activity in rat's liver compared to the non-treated irradiated groups.

Conclusion: It seems that BME extract with antioxidant activity reduced the genotoxicity and cytotoxicity induced by gamma irradiation in bone marrow cells and liver in the rat.

Keywords: Black Mulberry; Ionizing Radiation; Micronucleus; Bone Marrow Cells; Liver Parameters.



Origanum Vulgare Leaf Extract Protects Mice Bone Marrow Cells Against Ionizing Radiation

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Abstract

Background: Ionizing radiation produces free radicals which induce Deoxyribonucleic Acid (DNA) damage and cell death. Origanum Vulgare Leaf Extract (OVLE) is a natural compound and its capability of scavenging free radicals and its antioxidant activity have been demonstrated by many researchers. In this study, using micronucleus assay, radioprotective effect of OVLE against clastogenic and cytotoxic effect of gamma irradiation has been investigated in mice bone marrow cells.

OVLE was injected intraperitoneally to the BALB/c mice 1hr prior to gamma irradiation (3Gy) at the doses of 100 and 200 mg/kg. Twenty four hours after irradiation or treatment, animals were killed and smears were prepared from the bone marrow cells. The slides were stained with May Grunwald–Giemsa method and analyzed microscopically. The frequency of Micronucleated Polychromatic Erythrocytes (MnPCEs), Micronucleated Normochromatic Erythrocyte (MnNCEs) and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte + normochromatic erythrocyte) were calculated.

Materials and Methods: 200 mg/kg BME injected intraperitoneally to the forty-eight male wistar rats three days before and three days after 3 Gy and 6 Gy gamma irradiation, The frequency of micronucleated polychromatic erythrocytes (MnPCEs), micronucleated normochromatic erythrocyte (MnNCEs) and cell proliferation ratio PCE/PCE+NCE (polychromatic erythrocyte/polychromatic erythrocyte +normochromatic erythrocyte) were calculated. In addition, the level of malondialdehyde (MDA) and Superoxide Dismutase (SOD), total thiol content and catalase activity was determined in rat's liver.

Results: The results showed that gamma irradiation (3Gy) increased the frequency of MnPCEs, MnNCEs and reduced the PCE/PCE+NCE ratio in mice bone marrow compared to the non-irradiated control group ($p < 0.0001$). Injection of OVLE significantly reduced the frequency of MnPCEs ($p < 0.0001$) and MnNCEs ($p < 0.05$) and increased the PCE/PCE+NCE ratio as compared to the irradiated control group ($p < 0.05$).

Conclusion: It seems that OVLE with its antioxidant properties and its capability of scavenging free radicals and reactive oxygen species can reduce the cytotoxic effects of gamma irradiation in mice bone marrow cells.

Keywords: Radioprotective Agents; Micronucleus; Bone Marrow Cells; Whole Body Irradiation; Origanum Vulgare.



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The Effects of Chronic Noise Exposure on Hippocampal Neurons in Wistar Rat

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Abstract

Background: Chronic noise exposure may lead to neural hippocampus apoptosis. Also stresses may result in dark neurons.

The aim of this study was to determine effects of chronic noise on the hippocampus neurons of exposed rats.

Materials and Methods: In this study 16 male wistar rats were divided randomly into 2 groups, including exposure (N) and control (C) groups. 30 days after onset of examination, skulls of rats were opened to remove their brains. TUNEL and Toluidine blue techniques were used for examination of samples. The number of TUNEL positive and dark neurons in the hippocampus of both groups was counted and were compared.

Results: In comparison with control group, in hippocampus of exposed rats neural apoptosis and dark neurons were increased considerably ($P < 0.05$).

Conclusion: Apoptosis and dark neuron in hippocampus of rats can be caused by exposure to chronic noise.

Keywords: Chronic Noise; Broad Band (white) Noise; Hippocampus; Apoptosis; Dark Neuron.



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Simulation of Safe Parameters for Blood Brain Barrier Opening in Rat Animal Model

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Abstract

Background: The central nervous system is protected from foreign materials by the presence of the Blood-brain Barrier (BBB). As a result, the effective delivery of diagnostic or therapeutic contrasts to the brain tissue is prevented and the treatment of central nervous system diseases such as brain tumors becomes complicated. So far, different treatment methods have been used, such as invasive methods (like topical injection of the drug) and some non-invasive methods. Employing ultrasonic waves and injecting microbubbles into the bloodstream can cause the opening of the BBB without damaging the neurons in the sonication area. In this process, the stable cavitation of microbubbles applies force to the wall of the brain capillaries and causes an unstable opening of the BBB. In a study by Kobus et al. in 2016, safe parameters for the opening of the BBB in rats were presented. Using the results of this study, such as the frequency, pressure range, and duty factor of ultrasonic waves, the modeling of the vessel-blood-bubble system was done, and the pressure distribution and vessel wall displacement were determined, and they were introduced as safe factors in opening the BBB.

Materials and Methods: A microbubble inside a microvessel containing blood is modeled as a gas-fluid-solid system. Intravascular blood is considered a homogeneous, incompressible, and Newtonian single-phase fluid. Modeling was done with the finite element method using Comsol Multiphysics software (Comsol version 3.5-Stockholm-Sweden). In order to save the solution time, symmetric two-dimensional geometry has been used. Because the boundaries of gas-fluid and fluid-solid are moving after the radiation of acoustic waves, the Lagrangian-Eulerian Approach (ALE) moving mesh is used. Through dynamic modeling of microbubble fluctuations and using a Rayleigh-Plesset equation that governs it using safe parameters, which is the result of an experimental study, including the frequency of radiation waves of 690 kHz and the sonication pressure with the amplitude of 0.68-0.73 MPa, Duty Factor (DF) 1% and microbubble with a radius of 1.5 microns, the pressure exerted on the endothelial cells of the BBB was obtained. Also, the displacement of the vessel wall was determined. The intensity of acoustic was obtained from $I = (P_a)^2 / 2\rho c$ (ρ , c , and P_a are the density of the domain, the velocity of the ultrasound, and acoustic pressure amplitude, respectively). The Energy Density (ED) created in the environment due to the radiation of ultrasound waves was calculated from $ED = I \times DF \times t$.

Results: The energy density for safe parameters from the experimental study was obtained: 8.4 J/Cm² and 10 J/Cm², which can be a measure of the safety of other protocols. Figure 1 shows the geometry of the blood vessel including vessel wall, microbubble, and blood inside the vessel (Figure 1a) and sonication pressure with amplitudes of 0.66 and 0.73 MPa, frequency 690 kHz, and DF=0.01 (Figure 1b). Figure 2a shows the pressure exerted on the vessel wall and Figure 2b shows the vessel wall displacement in terms of time under the influence of acoustic waves with a frequency of 690 kHz and DF=0.01. The maximum displacement of the vessel wall 13.1 and 17.1 nm was obtained for the amplitude of radiation pressures of 0.66 and 0.73 MPa, respectively. When the microbubble is exposed to ultrasound waves, it starts to oscillate and microcurrents are created in the blood around the microbubble. Microcurrents put pressure on the vessel wall and cause the wall to move. If this pressure is greater than the safe limit, it causes bleeding, and if it is lower than the safe limit, the BBB cannot open.

Conclusion: The maximum pressure created on the vessel wall was obtained 20.66 and 24.34 kPa, respectively, for the amplitude of radiation pressures 0.66 and 0.73 MPa. This shows that the pressures in this range can open the blood-brain barrier without causing damage and in a reversible way so that the therapeutic agents are transferred out of the cerebral microvessel and into the brain tissue.

Keywords: Ultrasound; Microbubble; Blood Brain Barrier.

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Simulation of Safe Parameters for Blood Brain Barrier Opening in Rat Animal Model

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Appendix:

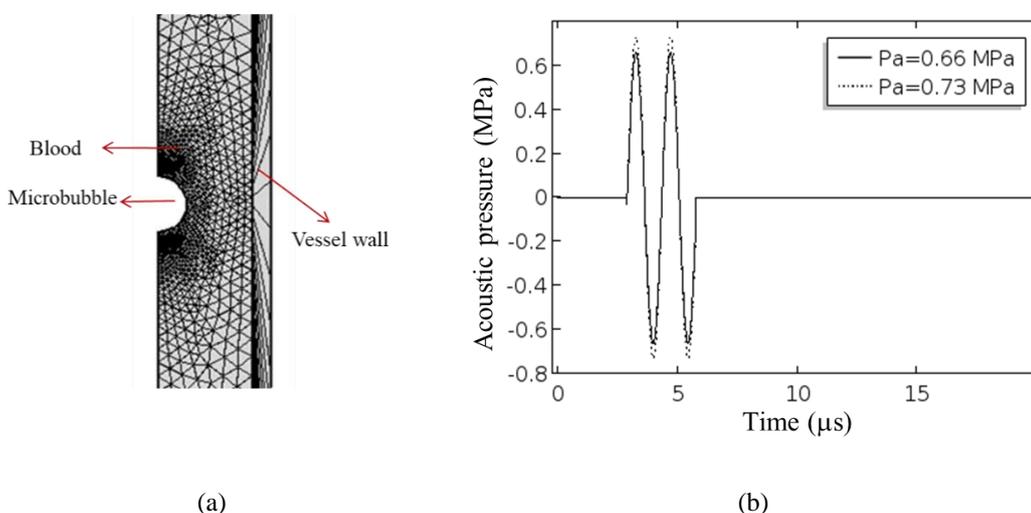


Figure 1. a) Modeling geometry including vessel wall, microbubble, and blood inside the vessel. b) Sonication pressure with amplitudes of 0.66 and 0.73 MPa, frequency 690 kHz, and DF=0.01

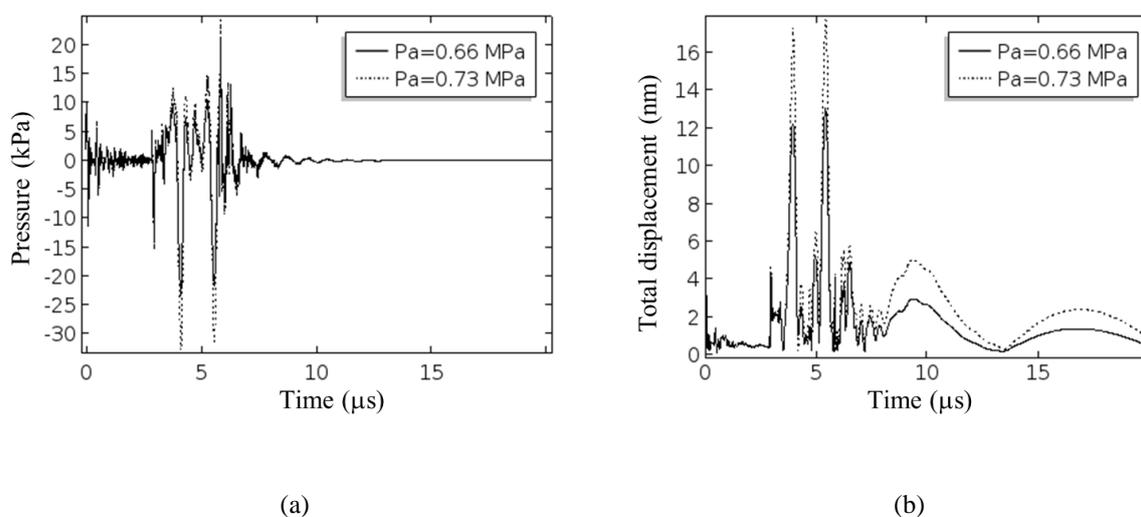


Figure 2. a) The pressure exerted on the vessel wall over time. b) vessel wall displacement over time



Evaluation of Glioblastoma Tumor Volume of MR Images with Modified Ellipsoidal Formula in Rat Animal Model

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Abstract

Background: Magnetic Resonance Imaging (MRI) is a common technique used to help manage patients with brain tumors, including glioblastoma. MRI is free of ionizing radiation, generally well tolerated, and provides detailed anatomic and functional information. Glioblastoma is the most aggressive and most common malignant primary brain tumor in adults, with high mortality and morbidity. To calculate the volume of tumors, including in animal models, the modified ellipsoidal formula is an accepted method. The modified ellipsoidal formula is a widely accepted method for calculating the volume of tumors, including in animal models.

In this research, the volume of glioblastoma tumors in male Wistar rats are compared using MRI and modified ellipsoidal formula.

Materials and Methods: To start the experiment, the animals were anesthetized by intraperitoneal injection of a combination of two drugs, ketamine and xylazine. The hair of the animal's head was shaved and the animal's head was fixed using a stereotactic device, and the animal cell line C6 GBM was injected into the animal through a Hamilton syringe. After two weeks of tumor induction, the animal was imaged using MR. For MR images, a 3 Tesla Siemens Magnetom Prisma scanner and an animal head coil with a holder were used in the National Brain Mapping Laboratory of Iran (NBML) and the images were taken with T2 Weighted settings in the axial direction. In order to obtain the volume of the tumor in MR, in all the sections where the tumor can be seen, ROI is drawn using image j software. The thickness of each section is set to 0.8 mm. As a result, $\sum_1^n 0.8 \times A_i$ is used to obtain the volume (A is the area of each ROI and i is the number of sections including the tumor). The modified ellipsoidal formula assumes that the tumor is in the shape of an ellipse and the height of the tumor is equal to its width. The formula is $V = 1/2 (a \times b^2)$, where V is the volume of the tumor, a is the length of the longest diameter of the tumor, and b is the width of the diameter perpendicular to the length.

Results: Figure 1a is a 3D image reconstructed from MRI by RadiAnt DICOM Viewer software (Medixant, Poznań, Poland) software. Figure 1b shows the MR image of the skull containing the tumor with the specified length and width. Correlation analysis shows a correlation of 0.98% between the tumor volumes obtained from MR images compared to the volumes obtained through the modified ellipsoidal formula (Figure 2).

Conclusion: The maximum difference in tumor volume obtained through ROI in MR images compared to the volume obtained using the modified ellipsoidal formula is 15%, and in all samples, the volume obtained from the formula is smaller than the volume obtained through ROI in MR images. The correlation between these two methods was 0.98%, which shows the compatibility of these two methods.

Keywords: Magnetic Resonance Imaging; T2 Weighted; Glioblastoma Multiform Tumor; Modified Ellipsoidal Formula.



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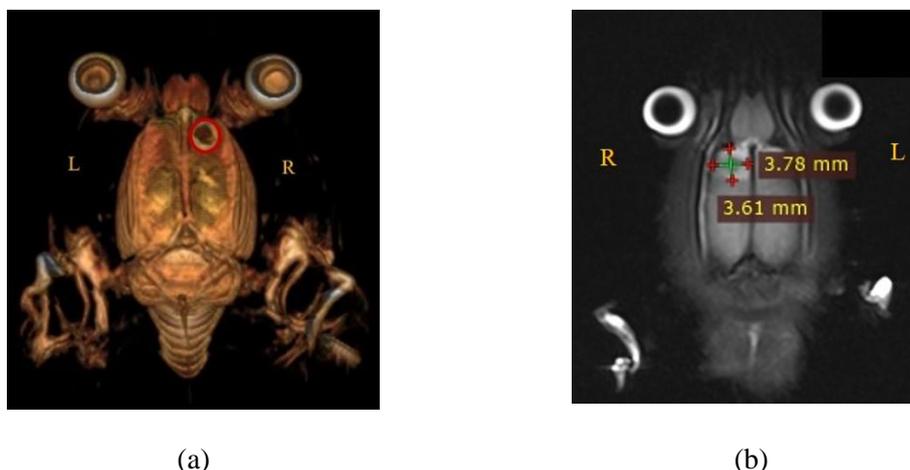


Figure 1. MR images of rat skull. A) ROI of tumor in a 3D image. b) Tumor dimensions

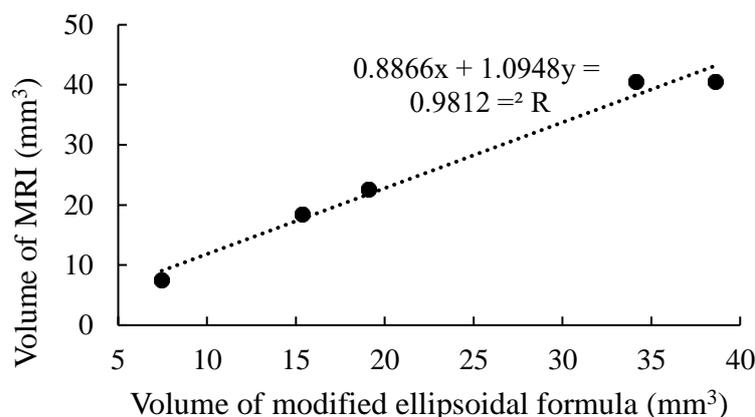


Figure 2. Scatter plots demonstrating the correlation between tumor volume measured by MRI and the modified elliptic formula