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CAPABILITIES OF WHOLE BODY MAGNETIC-RESONANCE TOMOGRAPHY IN DIAGNOSTICS, STAGING AND EVALUATING THE TREATMENT EFFICIENCY OF LYMPHOMAS (LITERATURE REVIEW)

The aim of this literature review is to assess the capabilities of whole-body MRI in diagnosing, staging, and evaluating the effectiveness of lymphoma treatment.
The results obtained give reason to consider MRI as a method with identical capabilities with CT and PET/CT for diagnosing, staging and evaluating the effectiveness of treatment in lymphomas.
Keywords: *whole body magnetic resonance tomography, lymphoma*

Introduction. Lymphomas are the tumors formed from lymphoid tissue, located outside the bone marrow [1]. Lymphomas make up 5-6% of all malignancies in adults, and up to 10% of cancer diseases in children [2]. Malignant lymphoma is the most common primary hematopoietic malignant tumor, as well as one of the most treatable forms of cancer. The two main categories of lymphomas include Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). The exact initial diagnostics of lymphoma is decisive for proper treatment planning and prognosis. Radiology methods (CT, PET-CT with 18-FDG, MRI) play an important role in the initial staging of lymphomas, evaluating the effectiveness of therapy and detecting recurrence of the disease [3-8].

Materials and Methods. The literature research was conducted on the PubMed database for the last 15 years (2003-2018) by keywords «Whole-body MRI, Lymphoma». This literature review includes 30 literature sources matching the selection criteria – these are full-text scientific articles containing the analysis of whole-body MRI results in lymphomas in comparison with other methods of radiation diagnosis, such as CT and PET-CT.

Literature review. CT is the most widely used radiological method for lymphoma staging due to its wide availability and a relatively low cost. Main CT-criterion indicating the lesion of lymph nodes is the change in their size. Pathologically changed lymph nodes are longer than 15 mm and/or wider than 10 mm [9, 10]. Total sensitivity and specificity of CT at node lesions above 15 mm in size reaches 87.5 and 85.6%, respectively [10-12]. It should be noted that the main limitation for the initial staging of malignant lymphomas using CT is the low level of informativity of this method with nodal lesions smaller than 10-15 mm in size. It increases the probability of false positive conclusions in case of a benign lymph nodes hyperplasia and lymphadenopathies of another genesis in children [13].

In lymphomas, morphological changes can fall significantly behind rapid functional changes; therefore, CT is not an ideal diagnostic tool in assessing early response to systemic therapy [8, 9, 10, 12]. In addition, CT is not applicable to the re-staging of lymphoma after completion of a course of treatment due to low informativity of this method in defining persisting viable tumor cells in large residual tumor masses [9, 11, 12]. PET-CT with 18-FDG is based on the fixation of positron decay of radiopharmaceutical drug which actively accumulates in foci with increased glucose consumption. Any foci with increased 18-FDG consumption in relation to the background tissue in the absence of benign hypermetabolic disorders is considered positive for malignant lymphoma. A meta-analysis of several prospective studies has shown that PET sensitivity and specificity in the staging of malignant lymphomas and the assessment of their response to treatment leave behind the sensitivity and specificity of contrast CT [14, 15]. The main factor defining the intensity of 18-FDG accumulation in a tumor, is the histological type of the tumor. HL and aggressive types of NHL are known for their high level of glycolysis that means a high intensity of the drug accumulation in tumor foci. Moderate and low levels of glycolysis and the relevant low intensity of 18-FDG accumulation in the tumor tissue are typical for indolent NHL. PET is an efficient method for detecting a lymphomatous lesion regardless of its size, as well as to detect active tumor cells in the residual tumor masses after completion of the course of treatment [14, 16, 17]. Several large-scale studies have proven PET-CT to be more accurate method of staging and re-staging of malignant lymphomas than contrast CT [18, 19].

The disadvantage of PET, and especially PET-CT, is their relatively high cost that makes both methods most costly in radiation examination [20].

During treatment and future dynamic follow-up, patients with malignant lymphomas have to undergo multiple cycles of CT and PET-CT examinations. As a result, they accumulate a significant dose of ionizing radiation, even in case of a low-dose CT. It can promote the risk of secondary tumors in the future [6-8, 10]. These reasons raise interest in MRI as an option without radiation burden. MRI creates an alternative to CT and/or PET for the staging of malignant lymphomas and dynamic follow-up during treatment [10, 21]. The main advantage of the whole-body MRI is the possibility to obtain full image of the pathological process spread in the body (lesions of lymph nodes of bone marrow and other organs) within one examination. Recent studies show that the whole-body non-contrast MRI protocols including diffuse-weighted images (DWI) can be used for the initial staging of lymphomas [7, 22-28]. Magnetic resonance diffusion is a method that allows determining the translational movement of intracellular water molecules in the tissues. DWI MRI has high potential in assessing malignant lymphomas. Quantitative measurement of the diffusion degree (according to the distribution maps of the proper or apparent diffusion coefficient (ADC)) can help distinguish malignant and benign lymph nodes [5, 8, 24-28]. In staging of malignant lymphomas, DWI is a valuable addition to the standard MRI protocols. DWI allows visualizing and measuring of the extra-, intra-and transcellular movement of water molecules due to their intrinsic thermal energy. The degree of freedom of movement of water molecules depends on several characteristics of the tissue such as cell packing density, the number of water molecules in the extracellular space, the concentration of protein and peptide molecules, the viscosity of the medium, and the presence of tissue necrosis. Limited diffusion is characteristic for most malignant tumors including malignant lymphomas. The use of DWI allows obtaining high contrast between the lesion focus and the background tissues which facilitates the detection of pathological foci [24-29]. Starting from 2008, many publications were devoted to incomplete and

small studies of the results of using whole-body MRI for lymphomas. According to preliminary data, MRI sensitivity and specificity in detecting node lesions in malignant lymphomas reach 98-99%, in extra-nodal lesions – 91-99%. According to preliminary results of a range of incomplete studies, DWI can be potentially used (analog to PET) to differentiate clusters of viable tumor cells from foci of fibrosis or necrosis in tumor masses remaining after treatment [20].

Conclusion. Since the general prognosis for detecting lymphomas in the early stages of the development of the disease is quite favorable, the prevention of long-term complications associated with therapy and diagnostic procedures is an actual and important topic. All modern methods of anatomical visualization (Ultrasound, CT, and MRI) have a limited capacity of detecting metastases as they mainly rely on low-sensitive "size-anatomical" criteria. A hybrid PET-CT has high diagnostic accuracy and is gaining popularity as a method of visualization, initial staging, and assessment of evaluating the efficacy of treatment of aggressive malignant lymphomas. CT and PET-CT currently used to diagnose lymphomas are associated with exposure to significant ionizing radiation therefore attempts shall be made to reduce the exposure rate. Whole-body MRI and DWI (especially, with ADC) seem to be an effective alternative to CT and PET. A direct comparison of DWI and PET results is required to define if functional information obtained from DWI can replace PET. MRI can be especially useful for certain groups of patients like children, pregnant women, individuals with increased risk of complications from the administration of contrast agents. Moreover, MRI can become a method of choice for patients with an 18-FDG negative lymphoma. The value of diffuse-weighted MRI and ADC is not yet established finally. Today, PET is still required to evaluate the response to treatment. Whole-body MRI, being a relatively new radiation-free method of initial staging and evaluation of response to treatment in malignant lymphomas, becomes a widely available diagnostic option. It is shown that the integrated use of routine MRI methods with DWI and ADC can significantly increase the accuracy of diagnosis and this is the subject of current research.

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ЛИМФОМАЛАРДЫ ДИАГНОСТИКАЛАУДА, ЕМІНІҢ ТИІМДІЛІГІН ЖӘНЕ САТЫЛАРЫН БАҒАЛАУДА БҮКІЛ ДЕНЕНІҢ МАГНИТТІ-РЕЗОНАНСТЫ ТОМОГРАФИЯСЫНЫҢ МҮМКІНДІКТЕРІ (ӘДЕБИЕТТЕР ШОЛУЫ)

Түйін: Бұл зерттеудің мақсаты лимфомаларды диагностикалауда, емінің тиімділігін және сатыларын бағалауда бүкіл дененің магнитті-резонансты томографиясының мүмкіндіктері болып табылады.
Лимфома кезінде диагностикалау, сатылану және ем тиімділігін бағалау барысында алынған нәтижелер МРТ-ны КТ және ПЭТ/КТ-мен бірдей мүмкіндіктері бар әдіс ретінде қарастыруға негіз береді.
Түйінді сөздер: бүкіл дененің магнитті-резонансты томографиясы, лимфома

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ВОЗМОЖНОСТИ МАГНИТНО-РЕЗОНАНСНОЙ ТОМОГРАФИИ ВСЕГО ТЕЛА В ДИАГНОСТИКЕ , СТАДИРОВАНИИ И ОЦЕНКЕ ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ЛИМФОМ (ОБЗОР ЛИТЕРАТУРЫ)

Резюме: Целью настоящего исследования является оценка возможностей МРТ всего тела в диагностике, стадировании и оценке эффективности лечения лимфом. Полученные результаты дают основания рассматривать МРТ, как метода обладающим идентичными возможностями с КТ и ПЭТ/КТ для диагностики, стадирования и оценки эффективности лечения при лимфомах.
Ключевые слова: магнитно-резонансная томография всего тела, лимфома